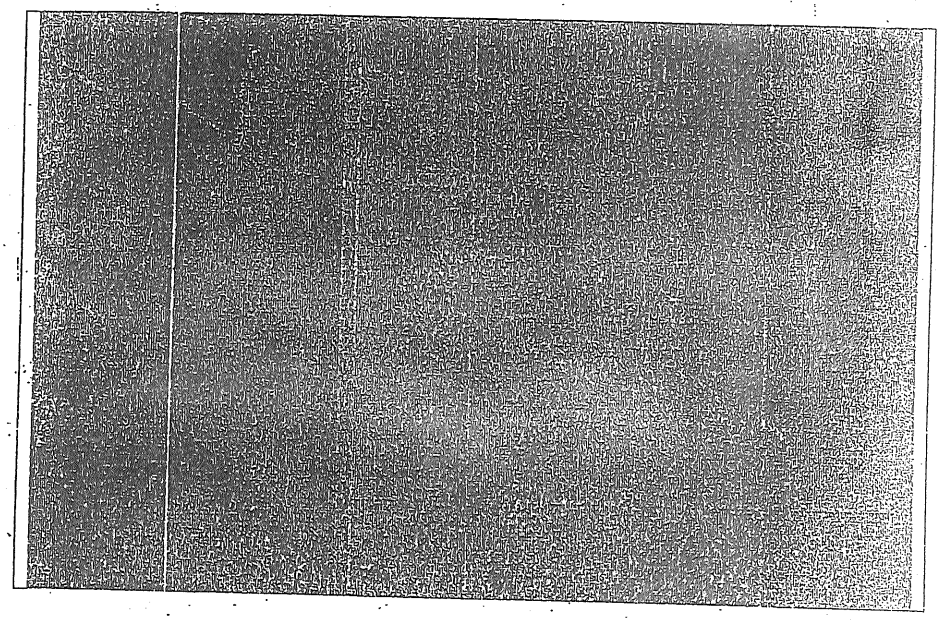


Acne Vulgaris

By
Dr. Hany Abo Elwafa

SG

- Site. All except... maximum sites:
- SG ass. ? H.F Except....
- Type of sec.
- Types of AF acc. to Seb. G.
- (F) → Sebum ?? Stimulated of its src.
  (F) Structure +/+ &/--

Acne Vulgaris

(Basics)

- Sebaceous Gland (SG) = Pilosebaceous unit = Hair follicle.

A - Embryology: develop at 13-15 th wk. of gestation as Budding from ↓ primordial Follicular epith.

B - Histology:

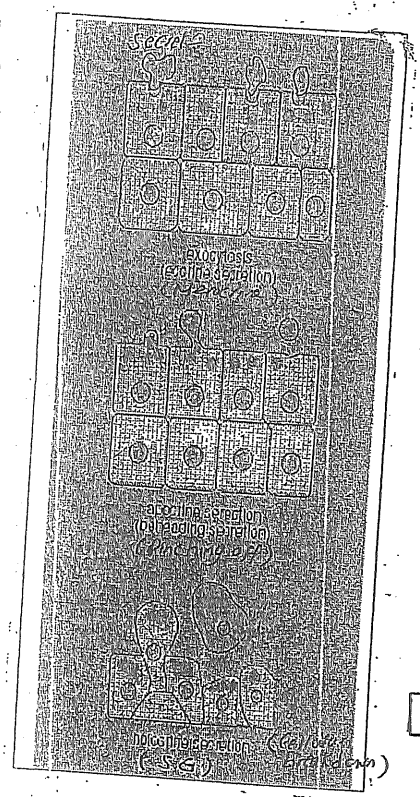
- Holocrine gland: secretion formed by complete destruction of the cells & Transit time 7-4 d
- ~~xx~~, formed → many lobes each ē a duct (lined by st. sq. epith.) → Converge Toward the main Seb. duct → open into the Pilosb. Canal whose Epith. is Continous ē Surface Epid. (Infundibulum) space at dreage.

C Sites: - All over the body except < Palms / Soles

- Maximum desity at Sebaceous site (acne sites.) = Forehead, Cheeks, upper chest & back (400 - 900 glands / cm^2)
- while other sites 400 / cm^2). ["T-Zone area" of Face.
- In All sites are ass. ē Hair follicles

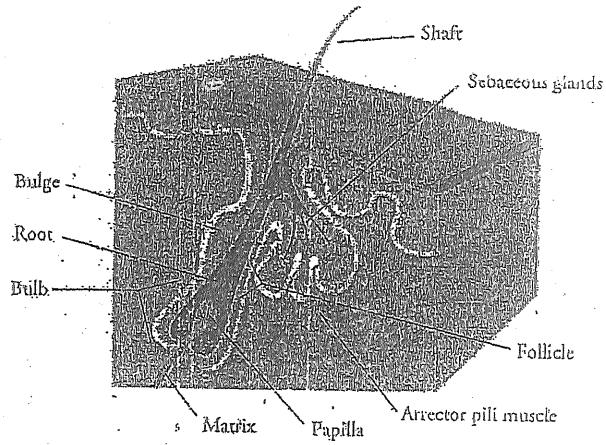
Except: (~~s~~)

- Meibomian glands: of Eyelids
- Montgomery Tubercles: of Areola.
- TySon's glands of Prepuce.
- Fordyce spots at Vermilion boder of lip & mm.

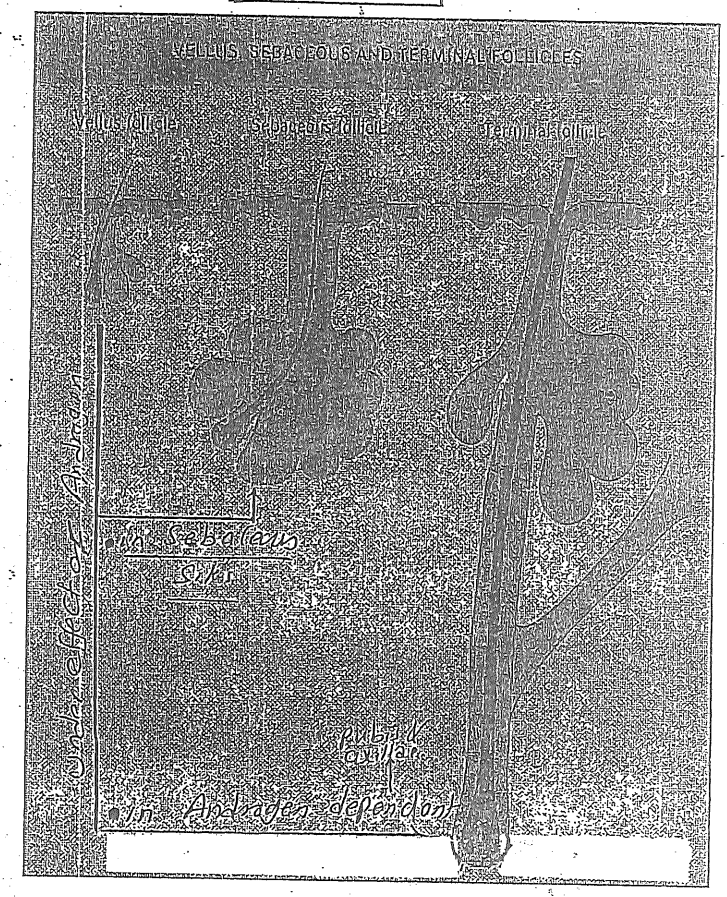


* Types of secretion.

D Types of SG (pilosb. units):



SG Types

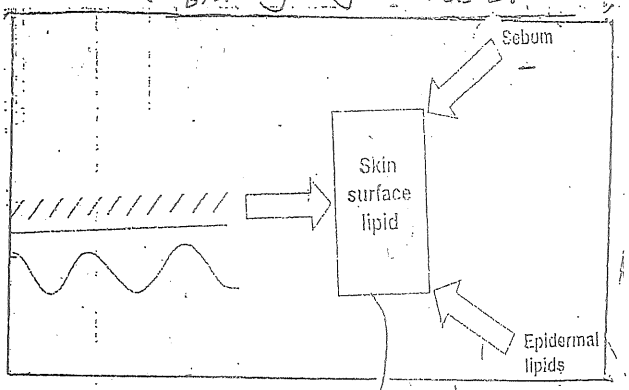


* *Vellus hair follicles:* with a short thin hair and small sebaceous glands
* *Sebaceous follicles:* with a midsized hair and large sebaceous glands; they are seen only in humans, especially on the face and the upper portions of the chest and back (the most common sites of acne vulgaris)
* *Terminal hair follicles:* with a long thick hair and fairly large sebaceous glands

Sebum Biochemistry

- Complex mixture of lipids that is secreted from the sebaceous glands.

- Sebum + Epid. lipids = Skin surface lipids (after Hydrolysis TGs by Lipases)
  - Sebum (from Epid. Keratinizate)
    - TGs
      - Cholesterol
      - Cholest. Esters
      - Wax esters
      - Squalene
    - as Sebum
      - But No
        - Squalene
        - wax esters
      - & much < TG, Chol.



- NB: Wax Esters & squalene:
  - are unique to seb. gland of Humans
  - also, not present in Epid. lipids & in lipids of internal organs
- (X) Squalene: in other tissues (Epid. & internal organs) → rapidly converted to Sterols ('cholesterol')

So, wax Esters & squalene are unique to S.G & To Human.

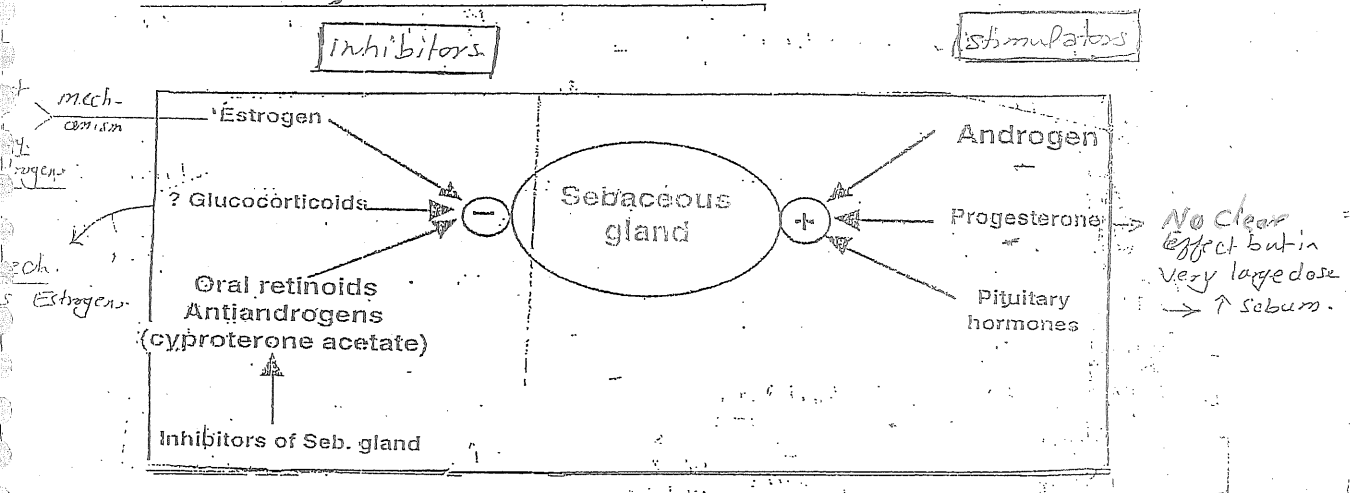
- as Sebum:
  - But there are FFAs (formed by effect of lipolytic enzs present in sebaceous ducts on TGs.

- Test:
  - S.G < Squalene / Wax esters
  - Epid. lipids: High conc. of TG < Cholest.
  - Skin surface lipids: FFAs.

- **Measurement of sebaceous activity**
  By placing a pad of cigarette papers for 3 hrs. on a limited area of forehead and then the sebum is extracted with diethyl ether.

- Function of Sebum:
  1. Moisturizer (↓ Epid. water loss).
  2. protective (d.t FFAs): against < Bacteria / Fungi (so T. Capitis "C in" Rare after puberty)
  3. Contain Vit E → antioxidant.

1. Control of Sebum Secretion (Endocrinal control)



- Androgen is the Main Stimulator for SG secretion

↓ So

- This the Cause of Hyperandrogenic Cut. diseases or SAHA synd.
(Seborrhea, Acne, Hirsutism & AGA)

- Basics of Androgen secretion & Metabolism
(Hirsutism أعراض)

- in Men Source of Androgen — Adrenal gland / Testes.
- in ♀ " " " — Adrenal gland, ovaries

- SG Contains 3 enzymes:
  - 3 β HSD (3 β Hydroxy steroid dehydrogenase)
  - 17 β HSD
  - 5 α reductase (II → all ducts & I → all gland lobes)

- at Adrenarche (7-10 y) → ↑ DHEA-S —3βHSD→ Androstenedione —17βHSD→ Testosterone —5-α reductase (I)→ DHT. (Androstenedione أو T من الكبد) → affect KCs & Sebocytes.

Acne Vulgaris

- **Def:** Chr., inflammatory disorder of Pilosebaceous unit
  - Cl- By formation of: Comedones (Dry lesions).
    papules / pustules
    nodules / cysts
    ± scarring

Epidemiology

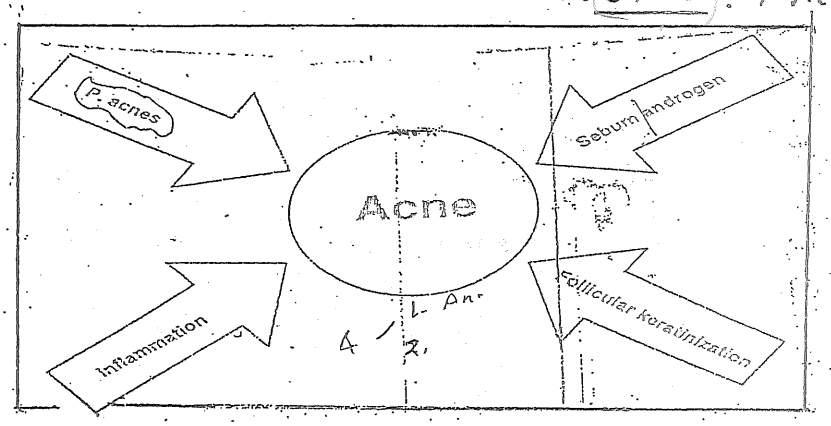
- **Incid:** 50% of Both Sexes.
  - **onset:** Generally 15–18 Ys (< Boys: 16–19 / Girls: 14–16 Ys); However Late onset ± Persist 20–35 Y (women)
  - **Resolve:** at mid twenties (usually < 25 Ys; However,
    - 12% of women
    - 3% of men
    ] may still have acne tnp 45 Ys

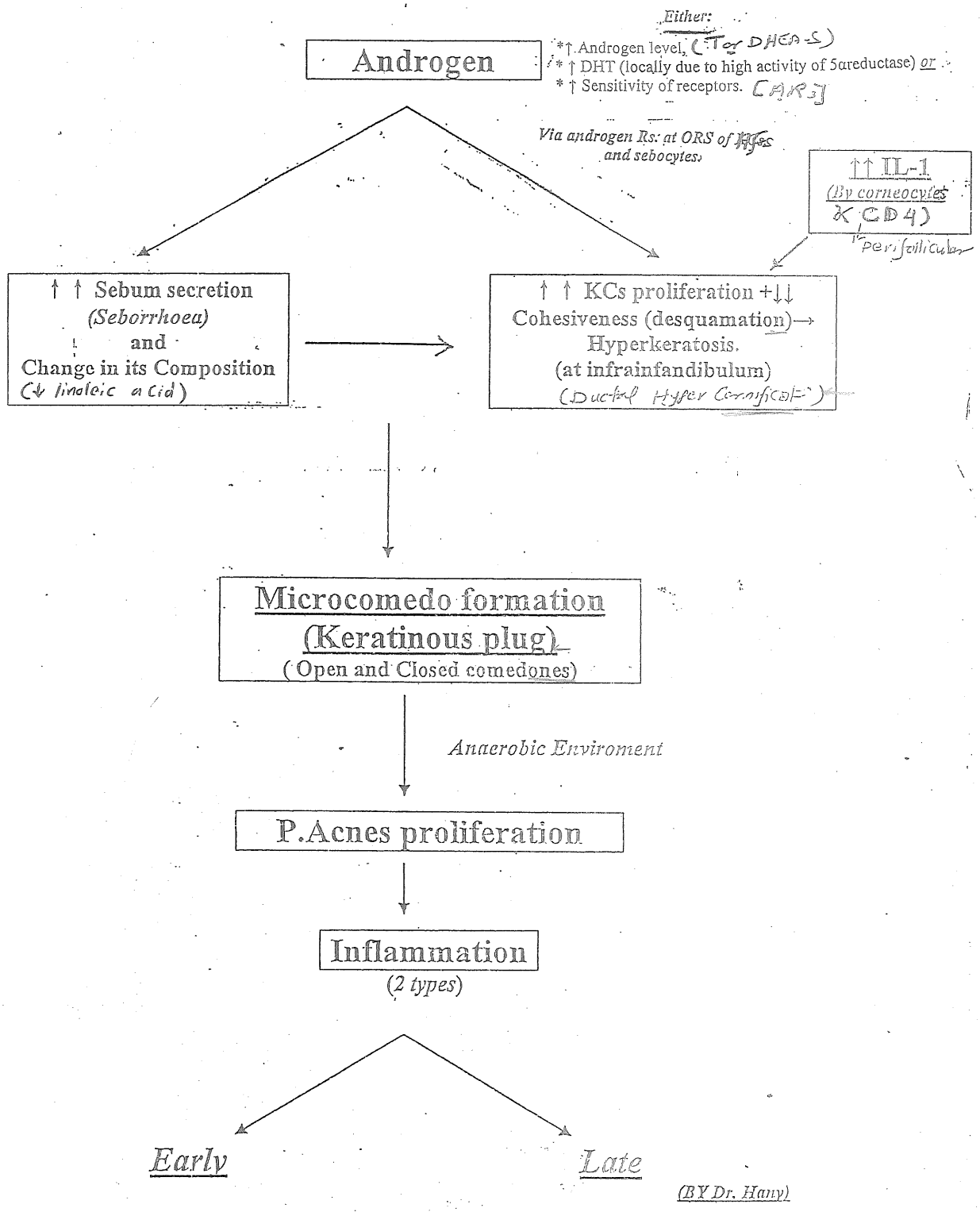
Pathogenesis (DA FP)

* 4 Key Factors: + other Factors:

1. ↑ Sebum (Seborrhea)
2. Ductal Hyperkeratinization ē Microcomedo formation.
3. P. Acnes, proliferate.
4. Inflammation.

- **Genetic:** +ve FH often ! present but definitive genetic data still lacking
- **Diet** (DA FP): Controversy but Recently: Hyperglycemic diet & milk & Junk food.
- **Premenstrual Flare:** 2–7 ds before Menses either d.t (↑ Progestin d.t hydrate of Pilosab. unit.
- **UVR:** may improve or Exacerbate acne (d.t ↑ Comedogenicity of Sebum)
- **Stress:** ↑ Acne (d.t substance P)




Either:
Androgen
*↑ Androgen level, (↑ of DHEA-S)
* ↑ DHT (locally due to high activity of 5αreductase) or
* ↑ Sensitivity of receptors. [AR]
Via androgen Rs: at ORS of Hyfes and sebocytes.
↑↑ IL-1
(By corneocytes & CD4)
Perifollicular
↑ ↑ Sebum secretion
(Seborrhoea)
and
Change in its Composition
(↓ linoleic acid)
↑ ↑ KCs proliferation +↓↓
Cohesiveness (desquamation)→
Hyperkeratosis.
(at infrainfandibulum)
(Ductal Hyperkeratinization)
Microcomedo formation
(Keratinous plug)
(Open and Closed comedones)
Anaerobic Enviroment
P.Acnes proliferation
Inflammation
(2 types)
Early
Late

(BY Dr. Hany)

NBs on pathogenesis

(1) Hyperandrogenic Cut. diseases May occur d.t:

1. ↑ Test. or DHEA-S levels (rare).
2. ↑ DHT d.t ↑ local activity of Enz. 5α reductase
3. ↑ Sensitivity of Androgen Receptors to NL Circulating levels of Testosterone or DHT.

(End organ responsible path.)

(2) Propionibacterium (Corynebacterium) Acnes:

- NL inhabitant of infundibulum (lower part).
- Anaerobic, Microaerophilic, Gram +ve rods.
- Produce Coproporphyrin III So:
  - show red fluorescence by W.L
  - Can be Targeted by laser light.
- Types: ① P. Acnes (commonest)
  - A
  - P
  - G.
  - ② P. Parvum
  - ③ P. granulosum
  - ④ P. avidum
  - ⑤ Propionicum.
- other diseases produced by Propionebacteria (see bact. Inf.)
- other diseases produced by P. Acnes:
  - AV
  - Progressive Macular Hypomelanosis
  - Acne Miliaris
  - Perioral dermatitis
  - Dental Inf.
  - Endocarditis
  - Conjunctivitis & Keratitis
  - brain abscess.
  - osteomyelitis.

HL:

Propionibacterium species are inhabitants of the skin and are usually nonpathogenic. As a result, they are common contaminants of blood and body-fluid cultures. These species are slow-growing, nonsporulating, gram-positive anaerobic bacilli and require at least 6 days for growth in culture.1 Propionibacterium species belong to the genera of coryneforms and are the best studied because of their association with acne vulgaris. found briefly on the skin of neonates, but true colonization begins during the 1-3 years prior to sexual maturity. During this time, numbers of P acnes rise from fewer than 10/cm2 to about 106/cm2, chiefly on the face and upper thorax. In the lipid-rich icroenvironment of the hair follicle, P acnes produces inflammatory mediators that result in papules, pustules, and later, nodulocystic lesions that are typical of inflammatory acne.

NB : organisms involved in AV (inhabitants of Hair follicle):

① Malassezia (at upper or acrum/mandib.).
② Staph. Epidermidis (at med. mandib.). (MSP)
③ P. acnes (at lower ").

(B) Inflammation: There are 2 Types of Inflamm. in AV.

even before Hyperkeratinization

→ Early (before rupture of ! Comedo) d.t:

[A] in Acne sites of genetically predisposed individuals, there are Perifollicular Presence of CD4 (T helper). That → IL 1α → follicular Hyperkeratinization & Microcomedo formation.

Late (d.t rupture of ! Comedo).

↓

it's d.t (P. Acnes) That produce:

↓

Enzymes as:
- proteases
- Hyaluronidases
- lipases (also act on Sebum → ↑FFa → ↑KCs prolif.)

↓

digestion of walls of Comedones

↓

liberation of their contents (Sebum, Keratin & bact.)

↓ FB reac°

Inflammat°.

[B] Chemotactic factors:

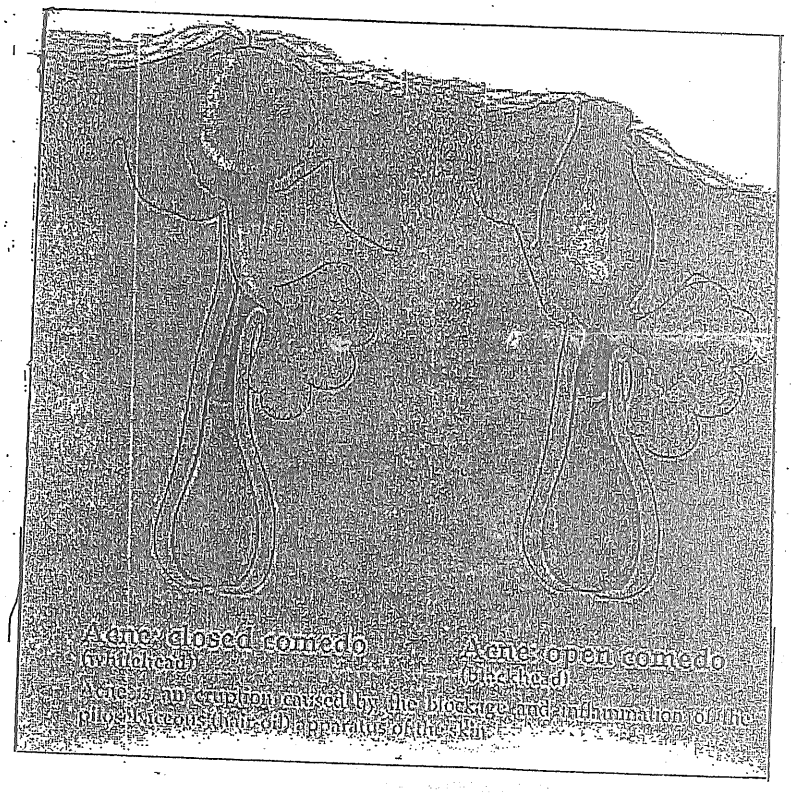
- P. Acnes → ++ Toll like receptor 2 (TLR2) on surface of Monocytes, Macrophages & PMNL → Chemotactic factors as:
  - IL1-α
  - IL8
  - TNF-α
  - PG like
  - ROS (by PMNL)

— Early Inflamm.

أول خلايا بتيجي هي Lymphocytes

(Papules Pustules Nodules Microcysts)

Fig. 37.1 Pathogenesis of acne.



CIP of AV

Classical AV

CIP
Grading

- lesions can be classified into:

1-Non-inflammatory lesions: (dry lesions).
Open comedones (blackheads)
Closed comedones (whiteheads)
Uninflamed nodules (sometimes called cysts)
2-Inflammatory lesions: Papules, Pustules and Inflamed nodules.
3. Secondary lesions: excoriations, erythema and hyperpigmentation, scarring.

- N.B Comedones are dry lesions of Acne ... can be classified Acc. to

Size

1. Micro (not seen clinically)
2. Macro > 1 mm.

Level of obstruction

Open Comedones (Black heads)

- obst. is superficial
- Pore: Partially blocked & communicate ē skin surface → Sebum oxidation → black discoloration (also ± d.t. ↑ Melanin (not d.t dirtiness).
- dont progress to inflamm. lesions
- Easily Treated.

Closed Comedones (White head)

- obst. is deep
- Pore: is completely blocked dont communicate ē skin surface → No Sebum oxidation → No black discoloration
- pogress to inflamm. lesion.
- difficult to be treated.

- Site: Face < Forhead, cheeks, ± Nose, Ear (Comedones) > upper Chest & back, upper arm.

Acne Grading (No universally Accepted Method)

Easy Method (Clinic)

1. Mild → Comedones ± papules
2. Mod → as mild + papules + pustules.
3. Severe → as mod. + Nodules & Cysts.

- Acne Conglobata
- Acne Fulminans
- G-ve Folliculitis
- Neonatal Acne
- Infantile Acne
- Acne Mechanica
- Acne Excoriée ....
- Occupational Acne
- Chloracne.
- Drug induced Acne.
- Acneiform Eruptions.

[Acneiform Eruptions]

B). 2nd Classification: "Combined Acne Severity classification."

Combined acne severity classification (Leeventvil)	Definition
Mild acne	Fewer than 20 comedones, or Fewer than 15 inflammatory lesions, or Total lesion count fewer than 30 (<20, <15, <30)
Moderate acne	20–100 comedones, or 15–50 inflammatory lesions, or total lesion count 30–125
Severe acne	More than 5 nodules, or Total inflammatory count greater than 50, or Total lesion count greater than 125

<20 ,15, 30

>5 . >50 . >125 .

NB: Population-based and migration studies have suggested a correlation between diet and acne. Large, well-controlled, observational studies have demonstrated that diets high in dairy products are associated with an increase in the risk for and severity of acne. Researchers have found significant associations between all varieties of cow's milk and acne. The relationship between milk and acne severity may be explained by the presence in dairy of normal reproductive steroid hormones or the enhanced production of polypeptide hormones such as IGF-1, which can increase androgen exposure, and thus, acne risk. Recent findings also describe an association between a high-glycemic-index diet and longer acne duration. In addition, randomized clinical trials have demonstrated that a low-glycemic-load diet can influence hormonal levels and improve insulin sensitivity and acne. No study has established a positive association between acne and chocolate, saturated fat, or salt intake. [Skin therapy letter; 2012]

. Also: Acne ↑ ē Junk Foods (بالإنجليزي)

Treatment of Acne

1. General Measures.
2. Specific Measures.
3. Ht of compliations.

A. Patient Education:

- AV is a physiological process that Needs prolonged & mentainance ## as long as it is present
- ## is For Control, Not For Cure (Except ē Isotretenoin)
- No improvement in AV before 6-8wks.
- Avoid milk, Emotional stress (Squeezing of lesions)

B. Causes of ## failure: (2C, 2D)

- Bad Compliance. (Commonest)
- Drug Interactions. "AV"
- Drug resistance.
- Coexisting underlying problem. e.g Suprarenal Tm, PCOS

C. Assesment Acne Severity: By assesing

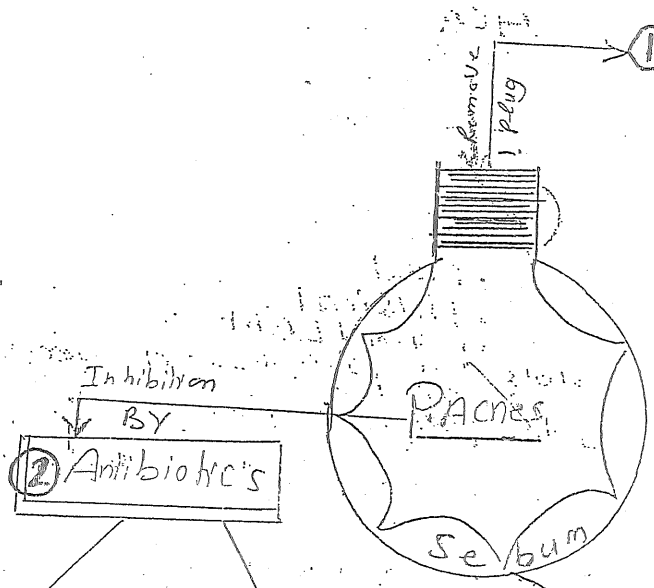
- Type (mild-med.-severe)
- Psychological condition
- degree of scarring

2. Specific Measures:

A. Medical ##:

علاج الأدوية التي تؤثر على AV

1. Remove the plug BY → "Comedolytics"
2. -- of P. Acnes → Antibiotics
3. ↓↓ Sebum → BY < Hormonal or Non H
4. Anti-inflammatory → BY: Adapalene, Azelaic acid, Antibiotics, Isotretenoin.



1. Comedolytics

- Salicylic acid
- Sulfur
- Resorcinol
- Retinoic acid derivatives: (Topical retinoid)
  - Tretinoin (RetinA)®
  - Adapalene (Differin)®
  - Tazarotene (Zarolax)®
  - Isotretinoin (Isotrex)®

(±)
- Azelaic acid (Skinoren)®
- Benzoyl Peroxide 5% (Panoxyl 5 gel) (BP)

Inhibition BY

2. Antibiotics

Topical
- Erythromycin
- Clindamycin
- Benzoyl peroxide (BP)
- Azelaic acid

Systemic
- Tetracycline
- Doxycycline
- Minocycline
- Erythromycin
- Azithromycin
- Clindamycin
- TMP+SMX (Septrin)®

3. ↓ Sebum BY:

Hormonal ++

Non Hormonal → Isotretinoin

BY

Anti-Androgens
- Cyproterone acetate
- Spironolactone
- Cimetidin.

Androgen inhibitors
- low dose dexamethasone
- OCPs
- GnRH analogs
  - Finasteride
  - Dutasteride.

The following drugs have double Act:

1- B.P < Antibacterial (++) (mainly) / Comedolytic (+)

2- A Zeliac : antibact. & Comedolytic

Remove the plug By comedolytic

1. Comedolytics

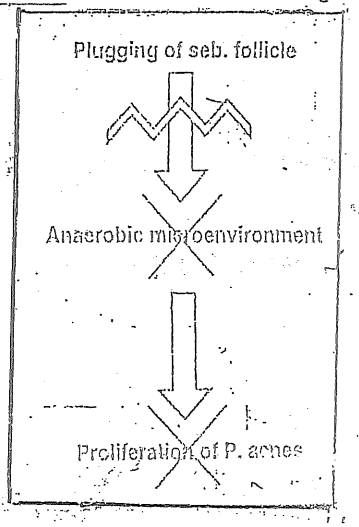
- salicylic acid, sulfur & Resorcinol : old Comedolytics, not used commonly nowadays.
- Retinoids (Synthetic analogues of Retinoic acid)

A. Tretinoin (0.1%, 0.05% & 0.025%) → have 2 types of Receptors (for details see section of Retinoids).

- Cytoplasmic
  - CRABP (Cellular Retinoic acid Binding protein)
- Nuclear
  - RAR (Retinoid acid receptors)
  - RXR Retinoic X Receptors.

* Retinoids + CRABP —(Carry them to Nuc.)→ bind to Intranuclear Receptors on DNA → affecting differential gene expression

- Mechanism:
  1. Comedolytic
     - Treat already present Comedones
     - (b) Normalization of follicular Keratinization & ↓ Cohesiveness of abnl follic epith.
     - Prevent New Comedo formation
  2. Anti-inflammatory: -- leukocytes activity, -- Cytokines rele & -- Toll Like Rs.
  3. Facilitates penetration of other drugs.



معنى كلام
ترتيب
بدون
Retinoids.

S.E

1. Irritation (CD) to avoid:

- start ē cream base (لا يجب ... [illegible])
- ē lower concentration (0.025% → ↑)
- gradually ↑↑ application period. ← دهان نصف ساعة ثم شطف / تزاد ساعة كل اسبوع الى ان ... يوضع مساءً والشطف صباحاً
- gradually (↓) application interval → بالليل كل اسبوع / ثم ٢ ليالي / ثم كل ليلة (stepwise increments done every 3-4 wks)
- completely dry skin. (تنشيف الوجه بعد ساعة ينشف / نصف ساعة غسيل)
- تجنب الصابون & استعمال ...

2. Photo irritation:

- apply at Night & ↓ light Exposure.
- wash at morning & use sunscreen.

ليه نستعمله مساءً؟
1. To ↓ photo-irritat.
2. To ↓ its degradat. → "photo-labile"

3. pregnancy & Lactation: Category (C) so avoid it during ↑ (for medicolegal)

4. Acne exacerbation: during 1st (4 ws)
exacerbation may occur d.t Externalization of deep seated lesion..

Instructions:

1. دهان مساء كل يوم طبقة خفيفة مع عدم التعرض للضوء
2. شطف صباحا قبل الخروج ويوضع عازل شمس (بلا صابون – ماء بس)
3. ممنوع الدهان في ٣ مناطق: حول العين / زوايا الفم / Nasolabial fold → Irritat → hyper-pigm
4. مفيش نتيجة الا بعد: ٦-٨ أسابيع
   أفضل نتيجة بعد: ٣-٤ شهور
   يكمل عليه باستمرار.

NB. if Cream base is not effective → use Sol. or gel form (more effective)
- after a period of Cream base use → shift to Sol. or gel.

- Total absence of skin irritation should lead the physician to suspect that topical therapy is not being used correctly!!
- Transient stinging is a useful sign of adequate coverage.

- Adapalene 0.1% gel : differs from (Retin A®) in:
  - doesn't bind to CRABP but bind to the Nuclear receptors specially RAR β & RAR γ.
  - More effective > 0.025% Tretinoin gel.
  - Less irritant → well Tolerated
  - Light stable → Can be used at morning
  - More potent antinflammatory effect (double Act.)

(ع أفضلية على تريتينوين)

- Tazarotene 0.1% : may be used daily or short contact Therapy
  - Selectively binds to RAR γ & Not RXR.

NB: . Retin A: & Adapelene → Category "C" in pregnancy
. Tazarotene & Isotretinoin → Category "X".

Topical Antibiotics

2- inhibit of P. Acnes — By Antibiotics:

- Erythromycin → Antimicrobial + antinflamm.
- Clindamycin → Antimicrobial + antinflamm.
- (BP) Benzoyl peroxide 5% → " + comedolytic
- Azelaic acid → " + "

- Erythromycin & Clindamycin : (قواعد عند استعمالها)

"Area ## Not Spot ##" ← ① applied to the affected area Not to the lesion because the peripheral zone of the lesion will recieve sub-therapeutic concentration → bact. resistance.

② should be used + Zinc or BP → ↓ Bact. Resistance
(Zincomycin, Acne-Zinc) (Acne-Benz, Acnidu) → (BP + Erythromycin)

Erythromycin 4% Zinc acetate 1.2%

(B) . B.P & Azelaic → No Resistance.

- Erythromycin + Zinc : Zincomycin (Acne Zinc) lotion ®
  BP : Acne benz gel. ®

③ Should be the same Type of systemic antibiotic e.g. avoid dissimilar antibiotics.

- Benzoyl peroxide 5% : (Panoxyl 5 gel)®

2.5% – 20%

- double mechanism of Action (see before)
  - Antimicrobial: Bacteriostatic d.t liberation of free O.
  - Comedolytics & TG, Hydrolysis
- S.E
  1. irritation
  2. Bleaching of clothes & Hair (المخدة - الملابس الشعر)

- Azelaic acid (20%) (Skinoren, Ezalic)®
  - Def. → Naturally occuring dicarboxylic acid that derived from [P. ovale] [Malassezia furfur]
  - Mechanism: (No effect on sebum).
    - Acne →
      - Comedolytic
      - Antimicrobial
      - Antiinflammatory (↓ ROS release from Neutrophils)
    - Pigmentary disorders → Bleaching Effect (↓ Pigm.): affects the Hyperactive MCs not the NL.
    - MM (Malignant Melanoma) → Arrest MM progression.

SYSTEMIC Antibiotics

1. Tetracyclines
2. Erythromycin
3. Azithromycin
4. Clindamycin
5. TMP + SMX

Tetracyclines

(تحريري - تحريري) (Comprehensive 2010).

Classificat:-

Short acting	Intermediate acting	Long acting
(half life: 6-12 hrs)	(16 hrs.)	(18-22 hrs)
. Tetracycline	. Demeclocycline	1. Doxycycline → Hyclate / Monohydrate (Granudoxy tab)®
. oxytetracycline.	. Lymecycline.	2. Minocycline → Minocycline / Minocycline HCL

Mechanism of Action:

Antibiotic Mechanism

Bacteriostatic by -- bacterial protein synthesis Through binding to "30 S" subunit of bacterial ribosome.

So Active against:

1. G+ve (staph & strept)
2. G-ve (but < G+ve).
3. others:
   - P. Acnes
   - Mycoplasma
   - Chlamydia.
   - Rickettsia
   - spirochaetes
   - some Parasites.

Non antibiotic Mechanisms

1. Antiinflammatory: inhibit Neut. & Eos. chemotaxis
2. Anti metalloproteinases: (Enz. that -- Collagen & gelatin products). "Anti collagenolytic effect"
3. ↓↓ Angiogenesis. (ايه) ↓ Scarring
4. ↓↓ Apoptosis.

> (ليه) Tetracyclines in acne act By:
>
> 1. ↓ P. Acnes ⟶ ↓ inflamm.
> 2. direct (intrinsic) antiinflammatory.
>
> (Antibacterial & Antiinflamm.)

Pharmacokinetics:

1. Absorption:

- Tetracycline → لازم تتاخد ع معدة فاضية يعني (absorption)
  - its abs. impaired (chelate) by:
    - dairy product (منتجات الالبان)
    - (in Antacids) → Alum. hydroxide
      - Ca+ . Zn . Fe
      - bisthmus subsaligylate.
- ممكن مع او بعد الاكل . Doxy & Mino. → لا علاقة لهما بالاكل.

2. Half life:

- Tetracycline → 6-12 hrs. (short acting).
- Demeclocycline → 16 hrs. (intermed. ").
- Doxy & Mino. → 18-22 hrs. (long ").

3. Excretion:

- Via Kidney Except Doxy. (via GIT)
- So CRF → prolongs half life & Doxy. is the Safest with CRF.

NB: Tetracyclines are lipophylic & reach higher concentrations in nails & skin.

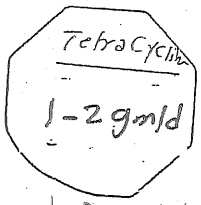
Indications (Dermatologic):

also used in Rx of: . urethra . pelvis . chest

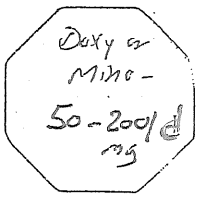
- **Common indications (Anti-P. acnes)**
  - FDA approved
    - AV (Minocyc. HCL For Rx of inflamm. non nodular acne in Pt > 12 ys)
  - Non FDA app.
    - ⓐ Rosacea.
    - ⓑ Perioral dermatitis.
    - ⓒ Hidradenitis.
- **less Common indications**
  - "Bullous diseases" → Tetracycline + Nicotinamide For Rx of:
    - PV
    - B.P
    - CP
    - DH
    - AIDs related KS
    - pruritic Pigment.

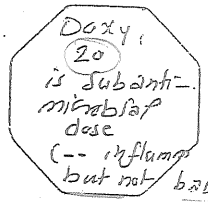
S.E

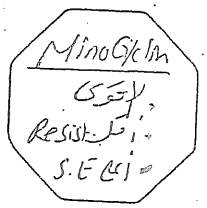
1. Tetracycline ← GIT candidiasis
2. Doxy → photosensitivity & onycholysis
3. Minocycline → Syndromes + Pigmentation
   - Skin
   - MM
   - teeth
   - Nail
   - Scalp
   - Generalized
4. Erythromycin: → GIT
   → ⊣ CYP 450
5. Clindamycin: Pseudomembranous colitis
6. TMP+SMX: SJS.



1-2 gm/d







S.E of Tetracyclines:

1. GIT effects: ⟶ to ↓ it take ē food (non dairy Products). [Doxy & Mino not Tetra]
   - Nusea
   - Vomiting
   - Epigastric burning.
   - Abd. discomfort.
   - Pancreatitis & Esophagitis.
   - Hepatotoxicity (sp. in large doses & in pregnant).

2. Renal: Fanconi Synd & progression of Uremia in patients ē renal dis.

3. Vestibular toxicity.

4. phototoxicity & onycholysis: (esp. Doxy & Demeclocycline).

5. Gram –ve folliculitis (after prolonged intake).

6. Children <9-12ys: "brown" discoloration of bone & Teeth & GR of bone. [permanent]
   "also Enamel Hypoplasia"

7. Minocycline:
   - SJS
   - Sweet's Synd.
   - depersonalization Synd.
   - DRESS drug Hypersensitivity Synd. (Fever, rash, LAN & AF)
   - SLE
   - Serum sickness like reaction.

8. other S.E:
   - Blue-black Hyperpigm. of skin, Nails, Teeth, Tongue, sclera.
   - Flaring up of Candidal vaginitis
   - Gynecomastia.
   - Pseudotumor cerebri (if + ISot.)
   - Phlebitis (if IV)
   - leukocytosis → atypical lymphocytes & ↓ Plat.
   - Neuromuscular blockade (S+ in MG).
   - Diabetes insipidus

Demeclocycline → Diabetes insipidus

- Contraindications:
  - pregnancy (Category D)
  - lactat^ (not safe).
  - Children < 9-12 ys (??)
  - Liver & renal impairment.
  - With iron, Ca, & dairy products of Antacids.
  - at bed time → Eosophagitis.

- Interactions: they:
  - ↑↑ Effect of → oral anticoagulants, Digoxin & Insulin.
  - ↓↓ " of → OCPs. [oral Contraceptives]
  - + Isotretinoin → ??
  - CYP450 Inducer.

- Dose:

Patients differ in the amount of tetracycline they need to control inflammatory skin diseases. A full daily dose of tetracycline is generally prescribed for the first few weeks or months to see how well it controls the skin problem. This full dose should be continued for most patients with acne. However, those with rosacea and perioral dermatitis may be able to reduce their dose at approximately monthly intervals.

- Tetracycline: 250-500mg four times daily (1-2 gm daily)
- Oxytetracycline: 250-500mg four times daily
- Demeclocycline: 150-300mg twice daily
- Doxycycline: 50-100mg once or twice daily (50-200 d)
- Lymecycline: 300-600mg once or twice daily
- Minocycline: 50-100mg once or twice daily (50-200 d)

There's a lag period of one to three weeks between the change in dosage and its effect on skin. If the skin problem becomes worse, return to the previous higher dosage and continue on it or as advised by your doctor.

Precautions

- TMP+SMX → Regular Strength: Backerim — SMX 400 mg / TMP 80 mg
  → DS = Septrin = 800 mg + 160 mg.

- Dose in Children — 40 mg/kg/d SMX
  8 mg/kg/d TMP

(2) ErythromyCin: → Main use in pregnant

. Dose: 1 gm/d : (250-500 / 4 hours)

. S.E: GIT upset & --Cyp 450

(3) AZithromyCin:

✓ Dose: . كبسولة (٥٠٠) يوميا لمدة ٣ أيام
ثم راحة ٤ أيام [علبة كل جمعة] لمدة شهر
(على معدة فاضية)

(4) ClindamyCin:

Dose: 300-450 mg/d

S.E: Pseudomembranous Colitis →

def.: Inf. of Colon BY Clostridium difficile ↓ N. flora affected

Manifs: . Abd. pain . diarrhoea . Fever . Toxic Mega-Colon ↓ Tt . VancomyCin . Flagyl.

(5) TMP (160) + SMX (800) (Septrine DS).

. Dose: 400-600 mg/d

. S.E: . BM -- . drug Eruption ← SJS/TEN (So of limited use). . pregnancy (D)

NB: Main use in Dermatology: G-ve folliculitis

تعطى لمدة ٣ شهور ثم تقل بالتدريج

فترة العلاج ٣-٦ شهور ولو مفيش نتيجة بعد ٣ شهور ← يوقف

Hormonal Tt of Acne (للإناث فقط)

(Antiandrogens & Androgen inhibitors)

↓ Sebum By ← Hormonal & non Hormonal Tt.

. Indications:

. Patients c̄ (Severe resistant Acne) that's not Candidate for (Iso-tretinoin).

- * Adult onset acne. [late onset]
- * Chr. Inflammatory acne (Painful, deep seated Nodules). ↳ "No Comedones"
- . premenstrual flare
- . distributed at ← Lower face, Jaw line, Chin.
- . Excessive facial oiliness (عايق)
- . Ass. other Androgenic manifs. (Hirsutism, AGA).

Clues of hormonal influence →

Antiandrogens & Androgen inhibitors

Androgen inhibitors

Inhibit Androgen production By:

- -- DHEA & -- T. production By
  - -- Supra-renal gland
    - low dose
      - Dexamethasone 0.5 mg
      - Ketoconazole.
  - -- Ovaries
    - CPs
    - GnRH analogs.
- -- of DHT production By
  - -- 5α reductase enz.
    - Finasteride (-- Type II)
    - Dutasteride. (-- Type I & II)

Anti-androgens

Block Androgen Receptors:

- Spironolactone
- Cyproterone acetate
- Flutamide
- progestrone
- Cimetidine

- Indications of Antiandrogens & And. inhibitors in Dermatology: (Disorders ē Excess Androgens)
  - Seborrhea
  - AV
  - Hirsutism
  - AGA (androgenic Alopecia)
  - Hidradenitis Suppurativa.

SAHA Synd (Dermatologic androgeni-zation Synds).

---

1. Spironolactone (Aldactone)®

- Mechanism
  - Main: -- ARs.
  - other: -- Androgen Synthesis (by -- ovarian & adrenal CYP 450) Also -- 5α-reductase
- Pharmacology:
  - peak level: 2-4 hrs
  - Bioavailability: 90% (after oral)
  - protein binding: 98%
  - Half life: 10-35 hrs
  - Metabolism: to active metabolite (Canrenone)

Antiandrogens & Androgen inhibitors

Androgen inhibitors

Inhibit Androgen production By:

- -- DHEA & -- T. products By
  - -- Suprarenal gland
    - low dose dexamethasone 0.5 mg (night)
    - Ketoconazole.
  - -- Ovaries
    - CPs
    - GnRH analogs.
- -- of DHT products By -- 5α reductase enz.
  - Finasteride (-- Type II)
  - Dutasteride. (-- Type I & II)

Anti-androgens

Block Androgen Receptors:

- Spironolactone
- Cyproterone acetate
- Flutamide
- progestrone
- Cimetidine

- Indications of Antiandrogens & And. inhibitors in Dermatology: (Disorders ē Excess Androgens)
  - Seborrhea
  - AV
  - Hirsutism
  - AGA (androgenic Alopecia)
  - Hidradenitis suppurativa.

Also!

SAHA synd (Dermatologic androgenization synds).

---

1. Spironolactone (Aldactone)®

- Mechanism
  - Main: -- ARs.
  - other: -- Androgen Synthesis (by -- ovarian & adrenal CYP 450)
    Also -- 5α reductase

- Pharmacology:
  - peak level: 2-4 hrs
  - Bioavailability: 90% (after oral)
  - protein binding: 98%
  - Half life: 10-35 hrs
  - Metabolism: to active metabolite (Canrenone)

• Indications, C.I., pregnasy: → الجدول

Box 23-3: Spironolactone Indications and Contraindications

FDA-approved dermatologic indications
(None specific to dermatology)

Other dermatologic uses (SAHA)
Hirsutism[16–26,34,35]
Acne vulgaris[27–31]
Androgenetic alopecia[32,33]
Hidradenitis suppurativa

Contraindications
Renal insufficiency—acute or chronic
Anuria
Hyperkalemia
Pregnancy
Abnormal uterine bleeding (AUB)
Family or personal history of estrogen-dependent malignancy*

Pregnancy prescribing status—category ~~X~~ (C)

* This would include breast, ovarian, or uterine malignancies.

S.E (A) as All antiandrogens has 2 Comm S.E.

- GIT
- ♂ – ??
- ♀ ↓

1. Irregular Menestruat⁻ (AUB)
2. Feminizat⁻ of ♂ fetus if given during pregnancy. → to avoid this → give ocps.

How to avoid?? [it may resolve in 2-3 m of H]

- ↓ dose (50–75 mg/d)
- ✓ adding OCPs
- Cycling dose:

(B) Hyperkalemia: "نادرة"

- Serious & most likely to occur in pt. ē renal insuffeciency.

(C) Gynecomastia. (in ♂)

(D) Estrogen dependant Mg e.g Controversy

(E) GIT Symptoms.

- Monitoring:
  1. K. level — "خصوصاً مرضى الكلى"
  2. B.P
  3. Wt.

- Drug interactions: (small list)
  - دوائين للضغط (K + ACE-I) — With (ACEI) & K^+ → Hyperkalemia
  - with Salicylates → ↓ diuretic effect.
  - With Digitalis → ↑ level of it

- Dosage & Form:

2 Forms → Oral / Topical

Oral:
- tab: 25, 100 mg — في السوق المصري
- dose in Adu: 50 - 200 mg
- "مع الأكل"
- يومياً أو ٢٥ يوم في الشهر

Topical:
- ٥% الكريم لصبيونات في أمريكا
- تستخدم في علاج حب الشباب
- لتقليل Sebum:
- لا توجد دراسات كافية عنه.

- Efficacy: in Ht of Hirsutism it is
  - Potent > Finasteride & less Potent < Flutamide.

---

2. Cyproterone Acetate:

- progestin derivative
- Mech.
  - Main: Antiandrogen. [-- ARs].
  - Other: Strong progestional Activity (-- FSH & LH)
- Indications:
  - FDA
    - BPH
    - cancer prostate.
    - ↓ libido in sexual deviate behaviour.
  - off label
    - See table of dermatologic indication..

• Forms & Dosage: Cyproterone acetate present either

Alone (AndroCure 10 & 50 tab) ✓

or Combined ✓ EE why?

(Diane 35 & 50 tab)

[2mg Cyp. + EE < 35 ug or 50 ug]

4. Contraceptives (CPs): 2 Types

A. Minipill → Contain progesterone alone (Progestin)

B. Multipill → Contain Estrogen + progesterone.

Estrogen:
- usually in the form of Ethinyl Estradiol (EE).
- All Estrogens acting as Androgen inhibitor by Many Mechanisms:
  1. ↓ GnRH Sec. → ↓ FSH & LH → ↓ ovarian T. products.
  2. ↑ SHBG → ↓ Free T.
  3. Direct ✱ Effect of T. on S.G.

Progesterone has 3 Types (the 1st Type should be avoided)

(1) ↓ Androgenic progestins: has marked Androgenic effects e.g. Norgestrel & Levonorgestrel. • MPA.

(2) low Androgenic Types:
- Gestodene.
- Norgestimate
- Desogestrel (more active)
- Norethindrone.

(3) Anti-androgenic Types:
- Drospirenone
- Cyproterone acetate.

OCPs:
- Yasmin
- Diane
- Drospirenone
- Cilest (Norgestimate) (FDA)
- Marvelone (desogestrel)
- Gynera [Gestodene]

Progestrone: Androgen — Inhibit (— FSH, LH) & reduce & antiandrogen (— AR)

Drospirenone 3 mg + EE { 30 µg → Yasmin / 20 µg → YAZ } -- AR, -- 5α reduct.

Spironolactone, a synthetic steroid, is an antiandrogen that competitively binds to androgen receptors, inhibits 5á-reductase activity, and reduces androgen biosynthesis. This agent, in doses of 50-200mg/day, has been shown to be efficacious for acne, although the trials have been small, and differed in dosages evaluated, outcome parameters, and reporting methodology.1 Drospirenone (DRSP) is a novel progestogen derived from spironolactone and has both antiandrogenic and antimineralocorticoid activity. DRSP 3mg has been combined with two different doses of ethinyl estradiol: 0.030mg for Yasmin®, Bayer HealthCare; and 0.020mg for YAZ®, Bayer Schering Pharma AG. Yasmin® was recently approved for the treatment of acne in Canada, while both formulations are available in the US. For antimineralocorticoid activity, the dose equivalence for DRSP 3mg is spironolactone 25mg.[6]

Flutamide : (62.5 - 125) ، S.E قوي ضد تأثير الهرمون

Flutamide is a non-steroidal androgen receptor antagonist indicated for the treatment of prostate cancer and has been found to be effective for treating hirsutism.[28-31]

Flutamide may be used for the treatment of mild to moderate acne. It should be used at low doses; 62.5 mg or 125 mg per day have been shown to be effective. The combination of OCPs and flutamide is likely more efficacious than flutamide alone.[32] In hirsute women with acne who were treated with OCPs, the addition of flutamide was significantly more effective than spironolactone.[33]

The potential for hepatotoxicity limits its use. However, no cases of fatal hepatotoxicity have been reported with doses less than 500 mg per day.[30] There have been reports of mild, transient liver impairment at doses ranging from 375-500 mg per day.[34,35] Women should remain on OCPs for birth control purposes as feminization of a male fetus can occur while on this medication. Patients should be off the medication for 3 months before conception.

"ممنوع حمل لمدة ٣ شهور بعد توقفه"

(قراءة) Contraceptives prescribed in AV (choice acc. to progesterone type).

FDA approved (٣ أنواع) (غير موجود في السوق المصري)

- Estrostep (EE + Norethindrone)
- Orthi Tri Cyclen (EE + Norgestimate)
- Yaz (EE + drospirenone). (وللا ٢٠) (٣م)

Non FDA but effective (شبه بعض yaz cc)

- yasmine (EE + drospiren
- Diane (EE + Cyp. A)

في مصر

- Cilest. (EE + Norgest.
- Marvelon (EE + Desoges

- **S.E of O.C.Ps:**
  1. **General** (d.t EE):
     - headache, nusea, w.t gain.
     - Breast Enlargement & Tenderness.
     - Thromboemboli
     - Moode Swings.
  2. **Drug interact & CPs Failure:**
     - CYP 450 inducers may → Failure (مثل): Rifampacin, Griseofulvin, penicillins & Tetra Cycli
  3. **Other S.E:** dementia, MI, Stroke, Cancer breast.

5. Gonadotropin Releasing Hormone Analogs:

(Leuprolide & Nafraline)

Both → initially ↑ FSH & LH for 2-4 wo then → sustained inhibition of FSH & LH → ↓ Androgen product by ovaries.

- dose: Leuprolide: 1 mg IM daily
  - Nafareline: 400 μg Intranasally / Twice daily.

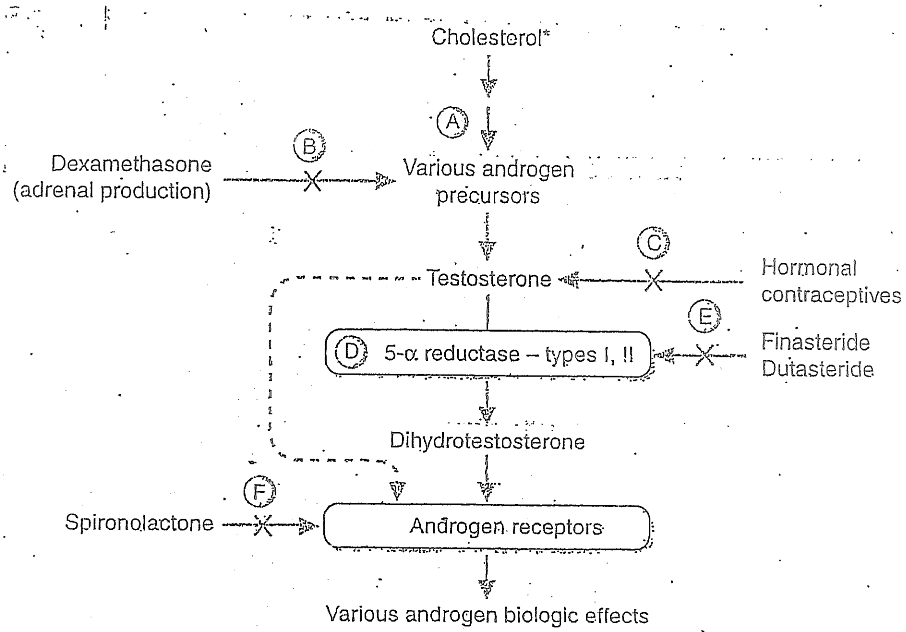
- disadv. Expensive & not well studied.

حلو

6. Herbal Remedies: (Antiandrogen & Androgen --).

- Saw palmetto
- + Green Tea. (تشرب شاي أخضر كثير كثير)
- Pygeum (AGA ← لتشجيع علاج بيرجيم). (60-500 mg/d)
- Stinging Nettle. (50-100 mg/d)

disadv.: Not proved by clinical Trials to be safe & effective.



* In mammalian cells, cholesterol is an essential cell membrane component (analogous to ergosterol in fungal cell membranes) and a precursor of all steroid hormones.
A Pertinent to androgenic steroids, cholesterol is converted to various androgen precursors such as DHEA and DHEA-S.
B **Dexamethasone** (and other corticosteroids) can inhibit the adrenal gland production of these androgen precursors.
C The ovaries can metabolize these precursors to testosterone; through negative feedback inhibition, **hormonal contraceptives** can ↓ ovarian testosterone production.
D 5-α reductase converts testosterone to its more biologically active form dihydrotestosterone.
E Both **finasteride** (type II 5-α reductase) and **dutasteride** (types I and II 5-α reductase) ↓ conversion of testosterone to dihydrotestosterone.
F Both testosterone and dihydrotestosterone bind to the androgen receptor; **spironolactone** competitively ↓ binding of both of these hormones to the androgen receptor.

Figure 23-2: Antiandrogen and androgen inhibitor mechanisms.

- Finasteride & Dutasteride → see AGA.

- NB: duration of Hormonal Rx ⟶ ≥ 3–12 ms.

Isotretinoin (systemic)
(13 Cis-retinoic acid)

Indications

1. Acne Vulgaris if:
   - Severe < nodulocystic
     massive inflamm. ⟶ scarring
   - Moderate: < Resistant or Relapsing ⟵ after 3 ms CB Conventa Combined Oral & Topical Antibiotics
   - Tendency for scarring.
   - Psychologically distress ful (Acne Excoriee) (Dysmorphic)

2. Acne variants: (Severe Types):
   - Acne Conglobata,
   - " Fulminans ⟶ "X-ray"
   - Hidradenitis Supp.
   - G-ve folliculitis.
   - Pyoderma faciale
   - Severe Acne Rosacea.

Mechanism (Acne)

↓ sebum production (also normalize linoleic acid level)
- Normalization of Follicular epith. desquamation. [Comedolytic]
- ↓ P. acnes.
- Anti-inflamatory

(Anti keratinization, inflamm, sebum, P. Acnes)

Dose: 0.5–1 mg/kg/d For ~ 5 months [4–6]
(till cumulative dose 120 mg/kg)
- Acne Conglobate: Need 2 mg/kg/d
- Start ē 0.5 mg/kg/d of start ↓ dose
  To avoid Flare:

Regimens

Continuous Regimen

- Indications: as before
- Dose: Start ē 0.5 mg/Kg/d for 1m (to avoid flare) & → ↑ gradually as the patient tolerate (max: 1mg/Kg/d) & Continue till a Cumulative dose **120–150 mg Kg / course**
- Course: 5 months (4–7 ms)

• يرتبط بنجاح العلاج : هو الـ ... :

Cumulative dose 120mg/Kg ω gives maximal Remission. (Now it's ↑↑ to 200 mg/Kg)

NB: Acne Conglobata: Needs 2 mg/Kg/d.

Intermittent Regimen

٣ أمور ← Indications:

1. mature adults ē late onset Acne
2. mild–mod. Acne
3. inability to Tolerate S.E of Continuous regimen.

- Dose: 0.5–0.75 mg/Kg/d

يومياً لمدة اسبوع ثم راحة ٣ اسابيع وتكرر العملية (لفترة ٦ شهور)

أو نفس الجرعة يومياً لمدة ١٠ أيام ثم راحة ٢٠ يوم [شهرياً كل شهر]

*** Effective**

- 80% → resolved
- 40% → relapsed after 1Y.

أو 0.3 – 0.75 mg/Kg/d For ≃ 6 ms

(Efficacy). The only Acne tt that's not open ended (leads to remission that lasts for ms – Ys).

- Results of one study after Isot. Course:
  - 40% → remains clear without tt for 3Ys.
  - 16% → Need Topical medication only.
  - 25% → 〃 oral Antibiotics
  - 20% → 〃 another Isot. Course.

- Relapse more common in:
  - Age < 16
  - Adult women
  - pts. with mild Acne.

→ Best Treat ē Hormonal tt

S.E (more details see Retinoids Therapy)

- Alopecia (T.E).
- Cheilitis → (90% ; most common لونا باستمرار و S.E)
- Dermatitis → مرطب باستمرار أو كورتيزون خفيف
- pruritus
- Pyogenic granuloma (Pseudo PG).
- Eye :: Xerosis (لازم تخلع العدسات وتستعمل Artificial Tear)
- Nose → Dryness → Crustation → Staph. aureus Colonization (90% of pts) (نستعمل فيوسيدين أو باسيتراسين حول فتحة الأنف أو ميوبيروسين)
- Depression, Psychosis & suicide.
- Arthralgia & Myalgia.
- Impaired Night Vision.
- Pseudo Tm Cerebri (داخلي)
- Pregnancy : Retinoid Embryopathy : abnormalities of : (50%)
  - Craniofacial (skeletal)
  - C.V.S
  - C.N.S
  - Thymus.

تأجيل أي عملية جراحية أو صنفرة لمدة سنة ↑ Tendency for Keloid.

Bone:
- Premature closure of Epiphysis (# الأطفال)
- DISH : Diffuse Idiopathic Skeletal Hyperostosis. (melted candle wax on X-ray)

- Lab abnormalities : ↑ Liver enzs . ↑ Lipids < TG (++) / Cholest (+) ± leukopenia.

(TGs ↑↑ more common)

C.I

- Pregnant
- Lactating
- Liver impairment
- Kidney
- Alcoholics (risk of Hyperlipid)
- DM
- Hypersensitivity
- Hypervitaminosis A
- Hyperthyroidism ??
- children (الصغار)

- منع الحمل أثناء العلاج والفترة شهر بعد وقف العلاج.

Drug Interactions

ممنوع مع :

- Vit A → Toxicity (But Beta Carotene may be allowed).
- Tetracyclines → Pseudo Tm Cerebri
- MTX → additive liver toxicity.

Pre ttt assessm. & Monitoring

- Pregnancy test : قبل العلاج ٢ اختبار ثم اختبار كل شهر
- CBC & renal : مرة كل شهر لمدة ٣ شهور ثم مرة كل ٣ شهور
- (2L.) Lipid < Cholest / TG , Liver : مرة كل أسبوعين لمدة شهر ثم كل شهر لمدة ٣ شهور ثم مرة كل ٣ شهور

NB

① Fatty meal لازم بعد.] بيزود امتصاصها للعقن
" " آكبر وجبة في اليوم

② لازم نبدأ بـ 0.5mg/kg يوميا
اول شهر
To avoid flaring of Acne

. if Flare occurs → : ?? — نبتدي بـ 0.25
. ↓ dose (0.25mg/kg/d) dr step
. Add Cs , 0.5-1mg prednisolone
For 2-3 ws. → slow ↓ over 6 ws

Risk of Flare
. Macrocomedones
. Nodules.

③ Presence of mucocut. S.E → indicate good abs.

④ Isotret ± given:
. For children & Neonates
. 5 courses ; ± Needed

. Slow Respone to Isot:
1. Macrocomedones → علاج Electrocautry.
2. Nodular Acne
3. persistent deep Pustules → علاج Antistaph antibiotic.

. Isot. Related Flare:
. Exacerbat^n of AV.
. A. fulminans → بنشيله بنقلل Cs وإعطاء Isot. ونوقف معاها
↙ "Paradoxical"

. NB: worsening of AV by ← Isot. ?? / Antibiotics ?? (علامتها)

تحذير - ضمان

iPLEDGE™
Committed to Pregnancy Prevention

Have Questions? Call our toll-free number 1-866-
Monday to Saturday, 9 AM - 12 AM (Mi

١. للطبيب اللي يكتب.
٢. للصيدلي اللي تصرف.
٣. للمريض اللي بيتعالج.

HOME
PATIENT INFORMATION
ABOUT ISOTRETINOIN
ABOUT iPLEDGE
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Find a Participating Pharmacy
FAQs

SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extrei high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amour even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. Ther are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This prograi called iPLEDGE™. Under this program, prescribers must be registered and activated with the iPLED(

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For Prescribers | For Responsible Site Pa

How to Report

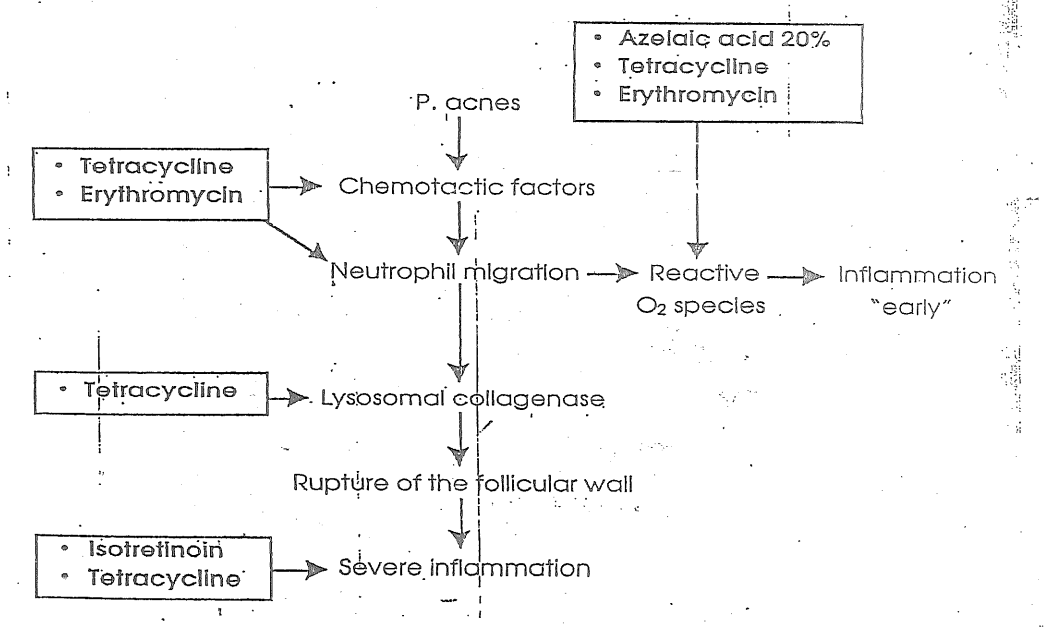
Call our toll free number 1-866-495-0654 to report any of the following:

An Adverse Event: If you or someone you know has experienced an adverse event, please 866-495-0654.

A Pregnancy: If you are an activated prescriber, report pregnancy results by logging in and on "Manage Patients." Otherwise, please call 1-866-495-0654.

(4) Anti-inflammatory effects of acne therapy

الحور الرابع للعلاج



2. Physical measures

- UVR
- Extraction of comedones: comedo extractor, light cautery after EMLA (local anaesthesia) application.
- Superficial freezing with liquid nitrogen.
- Intralesional corticosteroid injections (in lesions < 7 days old). → 2.5 mg/ml
- Cryotherapy. (lesions > 7 ds old)
- Cosmetic camouflage.
- post acne scars.

3 Lasers, Lights & Acne.

Mechanism either:

destroying P. Acnes through photodynamic reaction (PDT)

- Photoexcitation of Coproporphyrin III (produced by P. Acnes) → generate of Singlet oxygen (Free radicals) → destruction of P. Acnes.

- Types:
  1. Blue light sources (405-420 nm)
  2. Red light " : (660 nm).
  3. Combined Blue & red.
  4. Green light lasers. (582 & 532/1064)
  5. yellow " " (low fluence pulsed dye 585-595 nm)
  6. IPL
  7. Radiofrequency (RF) devices.
  8. PDT (Blue light & ALA).

- Blue light (intense violet) [405-420] → the best & approved by FDA.
- NLite Hi: (585)

destroy the Sebaceous glands

↳ PDL (by broad band light 550-700 nm)

- Types:
  1. near infrared lasers
  2. 1450 smooth beam lasers.
  3. IndoCyanin green (ICG) + diode laser (810-900 nm)
  4. 1540 Erbium glass
  5. RF devices.

Severe Acne:

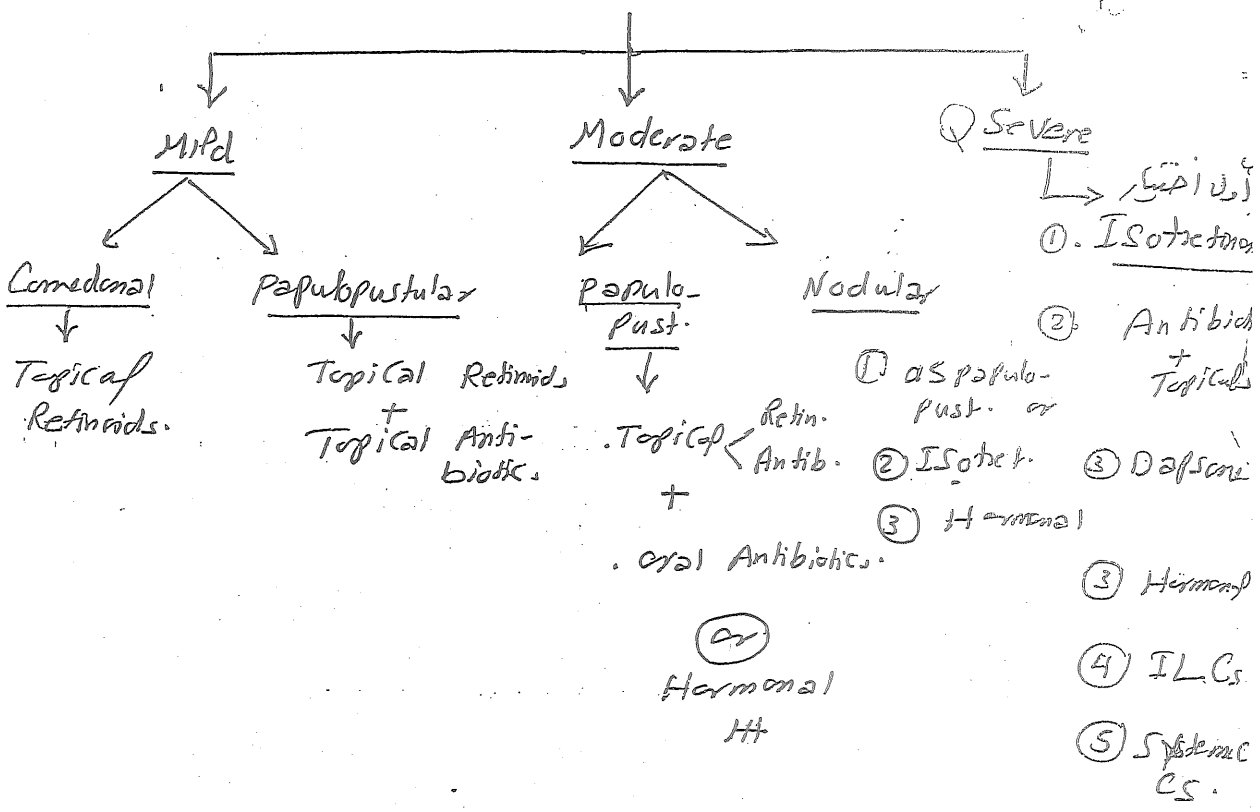
[1] Nodulocystic Acne (Acc. to
كمل, Severity (

laser / Light ##

بعد استعراض خطوط وأنواع العلاج

↓

هانختار العلاج على حسب درجة "Acne"



. Treatment of Severe Acne ?? (امتحان)

NB Nodulocystic lesions

- < 7 d. → ILCs (2.5 mg/ml : 0.025 @ 0.1 ml)
- > 7 d. → Cryo (2 Cycles; 15-30 sec.)

NB Cs in Acne

- **Acne & pregnancy:**
  - Pregnancy < Early: Exacerbate Acne
    late: ↓ Acne (d/t ↑ Estrogen).
  - **Safe drugs:** Erythromycin, BP, Azelaic acid.

- **Indications of Cs in Acne:**
  1. **Topical Cs:** for Severe inflammed papules.
  2. **IL Corticosteroid:** for Nodulocystic acne.
  3. **Systemic Cs:** for Acne fulminans.
  4. **low dose " ~ :** ↓ Suprarenal Androgens. (Dexameth.)
  5. ē Isot. to ↓ Flare

- **Non Isotretinoin tt ⇒ Nodulocystic Acne:**
  - 1. **Dapsone** (50–100 mg/d)
  - 2. **IL Cs**

- **Indications for Hormonal assessm. of Acne cases:**
  1. Irregular menest.
  2. Other androgenic Manifs. Hirsutism & AGA
  3. Rapid relapse after Isotretinoin.

5. Pyoderma faciale (Rosacea Fulminans).

HH

1. Isotret.
2. CS (Topic & Syst.)
3. Dapsone
4. Hormonal HH (♀).

Rx of Rosacea

A. Instruct (X Avoid)

- Hot, Humid
- emotional stress.
- Hot drinks.
- Alcohol.
- Spicy food.

Sun protect [illegible]

B. Manag of the Rosacea (Acc. to the type)

(i). Flushing: . B B, Clonidine, SSRIs

(ii). Telangiect: Laser, IPL

Brimonidine eye drops

(iii). Papulopust. Lesion

. low dose tetracycl (40 mg) /Day

Topical Metronidazol 0-75%-1% (Rosex)

"

Azelaic acid

(iv). ocular Rosacea:

Other lines

(1). Iverzine lot (FDA)
(2). Eflornithine.
(3). Cosmetics.
(4). Sulphur sol 1% in Calamine lot.
(5). Isot.
(6). Topical Anti
(7). Retinoids
(8). Flushing - Surgery

Rhinophyma

- Surgery.
- CO2.
- Dermabrasion
- Isotret.

FDA — Iverzine lot; Brimonidine

NB④ Bacterial Resistance in Acne.

- Common problem with AV.
- Classificat. Acc. to degree of Resistance:-

① Common
- Erythromycin.
- Clindamycin.
- Tetracycline
- Doxycycline.

(لو دوام بس / تحمل اللتين)

② Less Common
- Minocycline
- Zinc + Topical

③ No Resistance
- BP
- Azelaic acid
- Isotretinoid

- How to limit bact. Resistance in AV??
  - limiting durat. of tt.
  - Good Compliance.
  - don't leave the antibiotic Except if lost its efficacy.
  - (مهم) avoid use of dissimilar Topical & systemic antibiotics.
  - use Isotretinoin.

- NB2: what is Severe Acne,

① تعريف ممرض حب الشباب (Severe A. Vulgaris). Acne severity classif.

② A. Conglobata

③ A. Fulminans

④ G-ve folliculitis

⑤ Pyoderma faciale (Rosacea fulminans)

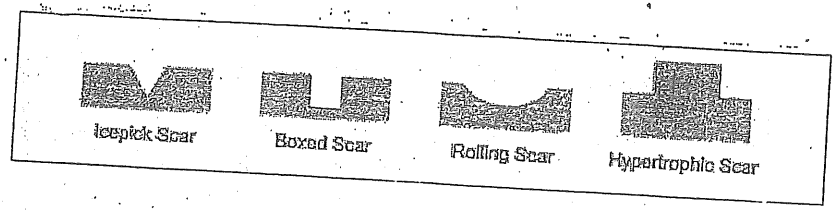
Complications of AV & its Management.

Psychological

1. depression
2. Dysmorphobic Acne. (disturbed Image)
3. disturbed social relationship.

Dermatological (SP | IS)

Post Acne scars. (4 types)



	Definition	Treatment
Ice pick scars (most common type)	pitted scars: It is due to the loss of part of the epidermis so that the skin 'dimples' slightly.	* Dermabrasion * Laser resurfacing * Punch grafting for deep scars. * Subcision®: a surgical (technique in which the fibrous band under the scar is divided, allowing the skin to return to its normal position). * Larger scars can be excised (cut out)
Atrophic scars (craters).	flat, thin scars. occurs when the epidermis is 'captured' by the scar tissue of a deeper acne lesion and is pulled into a deeper pit.	* Soft tissue augmentation techniques *such as* hyaluronic acid, collagen, gelatin matrix & fat implants * Dermabrasion
Hypertrophic(keloid) scars	thick lumpy scars	* Potent topical steroids for a few weeks * Intralesional steroid. * Silicone gel dressings * Cryotherapy * Surgical revision

- Solid facial Edema → Isotret + Ketotizen.
- Persistent Erythema → IPL
- Postinflammatory
  - Hyper Pigm. → Bleaching Creams
  - Hypo-Pigm. → leave For Time.

(NB Solid facial Edema: (Morbihan's dis.):

- An unsual & disfiguring complication of AV.
- C/P → · swelling & Erythematous non scaly woody induration of soft tissue of midline of the face & cheeks
  · No Spontaneous resolution.
- Causes: 1- AV
  2. Rosacea
  3. Melkersson Rosenthal synd.
- Rx → Isotret. (0.2-0.5 mg/kg) + Ketotifen (1-2 mg/d) for 4-5 m.

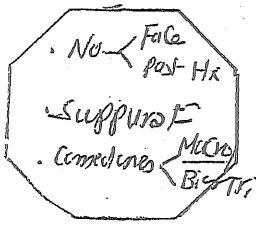
Etiology
damage to Lymphatics of face 2ry to AV

[≠ سلوليتس]
Cellulitis of Legs

[Complete Article on DOJ] (2008)

Acne Variants

1. Acne Conglobata:



- dpf. Severe Eruptive Nodulocystic Acne without Systemic manifestations.
- Usually affects males (20-25 yrs) with No Past Hx. of Acne.
- CIP: Severe Nodules, Cysts & Comedones (Macro (grouped bihead or Trihead) on Trunk (Face, back → large abscesses, sinuses, Keloids & Sca.
- Rx: 1. Isotretinoin 2 mg/kg/d For 5 mo.
  2. Corticosteroids (oral & IL)
  3. Dapsone.

NB: Acne Conglobata may be part of:

1. Follicular occlusion Triad or tetrad.
2. PAPA synd.
3. SAPHO Synd

Part of a related group of inflammatory disorders that include:
- Uveitis
- IBD
- PS

- Arthritis في AV مع التهاب:
  - A. Fulminans
  - PAPA Synd.
  - SAPHO "

4. PASH synd: PG, Acne, Suppurative Hidradenitis

1. **Follicular occlusion Triad:**
   - Acne Conglobata
   - dissecting cellulitis of scalp → Triad
   - Hidradenitis suppurativa
   - Pilonidal sinus → Tetrad.

2. **PAPA Synd:** Pyogenic arthritis + Pyoderma gangrenosum + A. Conglobata (or fulmin.

3. **SAPHO Synd:**
   - Synovitis
   - Acne (Conglobata or Fulminans).
   - Pustulosis
   - Hyperostosis
   - Osteitis.

Rx:
- Immunosuppressives
- Retinoids
- Infliximab

4. AHyS: Acq. Hyperostosis Synd.

PAPA

Threonine
↑
Interacting protein
· Genetic mutation in PSTPIP
↙ ↓ ↘
proline Serine phosphatase

or CD2BP1 gene. (Actin organization & maintain proper inflamm. response)

Acne Fulminans (Acne Maligna) = Leukemoid Reaction

- Most severe form of Cystic Acne that is ass. with systemic manifs.
- clinically: (sudden onset):

- Severe systemic manifs
  - FAHM
    - Arthralgia
  - Anemia
    - leukocytosis
    - ↑ ESR
  - HSM
    - Bone: → Osteolytic lesions.
  - Proteinuria & Haematuria

- Severe cut manifs. (Acne)
  - Early: Acne Conglobata like lesions
  - Later on: Hgic Nodules & plaques → suppuration & ragged ulceration (Hgic ulcer).
  - (face less affected)

Treatment

1. Hospitalization.
2. Wound
   - debridment.
   - Warm Compresses of 20-40% Urea
   - Topical Antibiotic.
   - Topical superpotent Cs.

- Systemic Cs (for 4 wks) (steroid)
  - till control → Add Isotretinoin
  - 2 wks → discontinue the Cs

0.5-1 mg/kg/d till Cumulative dose: 120 mg/kg

Isot.

Pathog.: Acute febrile systemic complic of Acne conglobata induced Immunologically by P. Acnes Ag & predisposed to by: Androgens, IMN, Isot.

	Acne conglobata	Acne fulminans
Sex	Men > women	Men
Age	20-25 years, Nos Past Hx	13-16 years & Past Hx
Onset	Slow	Sudden
Localization	Fac & Trunk	Trunk
Clinical features	Nodules, cysts, polyporous comedones	Hemorrhagic ulcerations
Systemic signs & sym.	Uncommon	Very common, malaise, fever, leukocytosis, elevated ESR, polyarthralgia, osteolytic bone changes, proteinuria, erythema nodosum, hepatomegaly, splenomegaly
Response to systemic antibiotic therapy	Yes	No

NB. ± ass c EN.

DD. Acne Fulminans like flare Induced by Isot.

3 Gram-ve folliculitis: (2015)

- or deterioration of ordinary Acne

- Superficial pustular or Nodulocystic eruption grouped around the ant. Nares occurs as a Complication of Prolonged ## of Acne with broad spectrum antibiotics (will colonize these bact.).

(i). follicular pustules
(ii). Nodular lesions
(iii). Worsening of Acne

- AET → G-ve bact. ← E-Coli, Pseudomonas, Proteus, Klebsiella. ← Enterobacter

- Treatment: 1. Stop the current antibiotics
  2. TMP: 400-600 mg id or Amoxicillin
  3. Isotretinoin: for resistant Cases.

For. Flora ... media ... sebum ...

- Etiopathogenesis:

(1) Antibiotic + Moisture (created by Sebum) → ↓ G+ve Flora (staph & diphtheroids) → ↑ G-ve bact. (from 1% - 4%) at ant. Nares.

(2) Hypersensitivity reaction to microbial Ag. (↓ IgM & ↑ IgE)

- Clin. suggestive History either:

(1) Nodulocystic AV. (e) non response to Antibiotic
2. Responsive AV → sudden flare following either cessation or reinitiation

- lesions either:

(1) Superficial pustules (cyst Comedones (80%) = Other G-ve bact.
(2) Deep Nodulocystic lesions → "Proteus"
(3) Generalized G-ve (e) Hx of Hot tubs or Swimming pools → (P)seudomonas

Ius: • G-ve Stain & Culture (selective Media of Methylene ↓ MB blue)
• Biopsy

→ Best by Isotret.?? has No Antibact effect but ↓ Sebum → ↓ Seborrhea → ↓ moisture → unfavorable environment for G-ve.

	4. Neonatal Acne	5. Infantile Acne
• Incid.	• 20% of healthy Neonate	• ♂ > ♀, ± FH of severe AV.
• Onset/ resolut.	• Start 1st 2 ws & resolve in 3 ms. (2wks - 3ms)	• Start: 3 - 6 ms & resolve in 1 - 2 ys (but) may persist to Adolescence.
• Cip	• Inflammatory papules on cheeks & nasal bridge • No scarring nor incid. of Acne later on.	• usually Comedones. • occassionally: Nodulocystic • ± scarring & ↑ incid. of Acne in later life.
• Pathogenesis	• Controversy: ± d.t 1. Malassezia (Furfur & Sympodialis) والدليل إنه بيحصل مع كيتوكونازول. So Some named it: ≪ Neonatal Cephalic Pustulosis ≫. 2. ↑↑ Sebum secret during this period.	may be d.t: 1. ↑ LH & T. during 1st 6-12 ms (طبيعي) 2. Immaturity of supra-renal glands → desp. Pertinately large Zona reticularis → ↑↑ DHEA-S (the level of ♋ ↓↓ at 1 year typ Adrenarche)
HH	1. reassurance (Self limiting) 2. Ketoconazole 2% Cr. 3. Benzoyl peroxide	1. Retinoids. 2. Benzoyl peroxide 2. ISot. (if Nodulocystic).

"Acne According to Age"

Age group	Location	Morphologic condition	Sex
Neonates	Nose, cheeks, forehead	Comedonal + papules	Both
Infants	Face	Inflammatory	Males
Preteens (childhood)	Centrofacial	Comedonal	Both
Teens	Face, trunk	Mixed	Both
Adults	Perioral, jawline, chin	Inflammatory	Women

"Postadolescent Acne" > 25 y.

Variants of AV
(Acneiform Erupt^n)

Type	C/P
1. A. Conglobata 2. A Fulminans 3. G-ve folliculitis 4. Neonatal Acne 5. Infantile Acne	→ See before
6. Childhood Acne (Juvenile) (2 - 7 ys)	• Etiology 1. Precocious puberty → Hormonal & Assay 2. Acne Cosmetica بيلطخ ادوات التجميل بتاعة مامته • C/P: Comedonal
7. Acne Mechanica	• occurs 2ry to repeated Mechanical Trauma To the pilosebaceous outlet ——→ obst. → Comedo format^n. • ممكن نلاقيه في شكل خط شبيه بالاحتكاك مع: • helmets كورة • bra straps • طرحة - إشارب • violins neck • لباتة Tt → Avoid Trauma
8. Acne Excoriee des Jeunes Filles (Pickers Acne)	• usually affects women c̄ Anxiety, depression or obsessive compulsive disorders. • C/P: 2 Types < No lesions or mild N (Comedones + Papules) → psychosis, anxiety squeezing, picking, scratching → linear & Geometric Erosions, Crustat^n & Scarring Tt < ① Psychotherapy ② Antidepressants [SSRIs, orap forte, Motival] ③ Acne Tt → Isotretinoin [aggressive Tt Needed]

X-Ray on Bone ??

Type	
9. Occupational Acne	Occupational Exposures to Comedogenic Substances e.g Cutting oils, (Coal tar) Petrolatum products [tar Acne] (في دباغ إيكاتيلية)
10. Chloracne	• Occupational exposure to Chlorinated Aromatic Hydro Carbons in: [• Electrical conductors & insulators. • insecticides, fungicides & herbicides. • Wood preservatives.] (دهانات) • C/P: Small cystic papules & Nodules at retroauricular, Manbibular, axillae scrotum. • Healing ± ⟶ Scarring. • H/ ① Stop the Exposure. ② Antibiotics, Retinoids & Isot. H/.
NB: Contact Acne: • Mechanica • Pomade • Cosmetica • Occupational (Tar)	
11. Pomade Acne (زيت عطرية)	نتيجة استعمال بزيوت وبكريمات دهنية على الشعر فتنزل على الجبهة (وجه جيد)
12. Acne Cosmetica (A. Venenata)	تتواجد في التجميل التي تحتوي على: Lanoline, Petrolatum, oleic acid ⟶ & Comedogenic Agents >>
13. Acne Detergents	→ d/t detergents e.g Hexachlorophene in Soaps ⟶ Papulopustular Erupt.
14. Acne Aestivalis (A. Mallorca) (Summer grage in North america)	• affect women in North america • Start in spring ⟶ Progress in summer & resolve in winter. • inflammatory papules (no < Pustules / Comedones) on cheeks & Neck.

15. Acne Medicamentosa

[Drug induced Acneiform Eupt]

سؤال امتحان

Differentiate bet AV & Acneiform Eupt:

AV is (Polymorphic)

- Abrupt onset
- Hx of drug intake.
- Not at classical sites of Acne (rare on face but at Neck, Trunk & arms).
- Monomorphous follicular papulopustular & Comedones (.. قليل أو معدوم) [Inflammed papules & pustules & Sparse-Absent Comedones].
- More common post-inflammatory Hyperpig. resolve & stop of drug.

Stop the drug

HF
- Tretinoin 0.05% ... (1-3 ms)
- Antibiotics.

(sudden flare) ظهور مفاجئ

Drugs reported to cause acne or acne-like eruptions (Acne medicamentosa)

Hormones and steroids
- Gonadotrophins
- Androgens
- Anabolic steroids
- Oral and topical steroids

Halogens (هاليدات)
- Bromides
- Iodides
- Halothane

Anti-epileptic drugs
- Diphenylhydantoin (phenytoin)
- Phenobarbitone
- Troxidone

Antituberculous drugs
- Isoniazid
- Rifampicin, Tetracycline

EGFRs inhibitors مثبطات

Miscellaneous
- Chloral hydrate
- Cyanocobalamin
- Disulfiram
- Lithium
- Psoralens (with UVA)
- Quinine
- Sulphur
- Thiouracil
- Thiourea

Vit < B1, B6, B12, D2

NB ① Cs: . Topical or systemic → Eupt:
. Systemic Mod-long Dekamedl.
For ≥ 3-5 ds → Eupt

② Cs Induced Acneiform ← Acne Rosacea, Acneiform Eupt

② Bromides: Sedative, Analgesic

③ Iodides: " " : Cold drugs, Vitamins, Contrast dyes.

3. Radiation Acne: "كويلت"

- Comedo-like papules d.t Exposure to ionizing Radiat°.
- starts to appear as the acute phase of radiat° dermatitis begins to resolve.
- Mechanism: Radiat° → epithelial Metaplasia in the follicle → Hyperkeratotic plug.

HL 4. Apert Syndrome [Acroencephalo syndactyly]:

- Androgen → ↑ AV, ↓ Early epiphyseal Closure.
- AD disorder ch: By disfiguring synostases of / bones of hands, Feet, Vertebrae & Cranium. (↓ Abn. joint development)
- This disorder may be ass. with Cut. manifs. as:
  - Seborrhea.
  - Nail dystrophy.
  - Hypopigmentation.
  - Acneiform Erupt°: (Extensive).
  - Nevus Comedonicus. ✓

d.t Mutat° in FGFR2 gene.

- Facies: Flattened occiput. ✓ Parrot-Beaked Nose.
- fused, shortened digits.

5. Transverse Nasal Crease: (pseudoAcne).

The transverse nasal crease is a horizontal anatomical demarcation line found in the lower third of the nose which corresponds to the separation point between the alar cartilage and the triangular cartilage. Milia, cysts and comedones can line up along this fold[33]. These acne-like lesions are not hormonally responsive and arise during early childhood prior to the onset of puberty. Treatment consists of surgical expression as needed.

6. Idiopathic facial aseptic granuloma :

A chronic, painless, solitary nodule, reminiscent of an acne nodule, appears on the cheeks of young children. The mean age at presentation is 3.8 years. Multiple lesions are uncommon. Histopathology reveals a chronic dermal lymphohistiocytic infiltrate with foreign body-type giant cells. Cultures are typically negative (70% of patients) and the lesions do not respond to antibiotic therapy. The nodules resolve spontaneously, after an average of 11 months, without treatment[33a].

سؤال امتحان

Syndromic Acne (Acne Syndromes)

- Follicular occlusion Triad / Tetrad
- PAPA
- PASH
- SAPHO
- Apert Synd.
- SAHA ✓
- PCO
- Apert.

. Other entities (By Bolognia):

1. Epidermal Growth Factor Receptor inhibitor:

. def. group of Therapeutic Agents used for Hx of Solid Tms (Glioblastoma, head & neck cancer and lung carcinoma) e.g 3 ← Gefitinib. Cetuximab. erlotinib.

• These Agents are ass. with Acneiform Eruption in most cases (≈ 75%) & it may indicate successful response to Hx.

• C/P: Eruptive Monomorphous follicular papules & Pustules involving face, scalp & upper trunk [No Comedones]

• Pathology: Folliculitis with intrafollicular Neutrophilic infilt. & perifollicular lymphocytic infilt.

• DD (Eruption in oncology patients):

1. Cs induced Acne.
2. Neutrophilic Eccrine Hidradenitis.
3. Folliculodystrophy of Immunosuppression.
4. other forms of folliculitis (Pityrosporum & demodex).

• Hx: Antibiotics, Cs (Topical) & retinoids.

2. Tropical Acne: حب الشباب

. Acneiform Eruption d.t Exposure to heat (in tropical climate) or 2ry to scorching حرق occupational Environment (as in furance فرن workers).

• C/P: Follicular Nodulocystic lesions ∴ may be infected by staph. at Trunk & buttocks

• Hx: → Moderate of Climate.

Causes of comedones

1. **1ry developmental defect of the follicle:** Nevus comedonicus and Nevoid follicular epidermolytic hyperkeratosis.
2. **A genetically determined abnormality of pilosebaceous function:** Acne vulgaris and familial comedones (autosomal dominant with mono- and poly-porous comedones and seb. cysts).
3. **Disturbed follicular keratinization** produced by exogenous acneigenic agents: Acne Venenata and Acne medicamentosa.
4. **Injury to pilo sebaceous follicles by ionizing radiation,** e.g. cobalt.
5. **Connective tissue abnormalities:** pseudoxanthoma elasticum, solar elastosis "Favre-Racouchout", lichen sclerosis et atrophicus, Necrobiosis lipoidica.

The spectrum of acne & acne-related dermatoses

Acne related to intrinsic causes
- Acne vulgaris
- Perioral dermatitis
- Acne conglobata
- Hidradenitis suppurativa
- Acne fulminans
- Pyoderma faciale

Acne related to extrinsic causes
- Acne excoriée des jeunes filles
- Acne mechanica
- Acne tropicals
- Acne aestivalis
- Favré-Racouchot syndrome
- Drug-induced acne
- Acne cosmetica
- Pomade acne
- Occupational acne
- Chloracne

Childhood acne
- Neonatal acne
- Infantile acne

Acneiform eruptions
- Rosacea
- Acne keloidalis nuchae
- Gram-negative folliculitis
- Steroid acne

Rosacea

(سؤال امتحان مهم جدا)

- def. Common Condition ch- By Symptoms of facial Flushing & a spectrum of Clinical Signs including Erythema, Telangiectasia, Coarsness of Skin & papulo-pustular Eruption resembling Acne.

- Etiology & Pathophysiology: → unknown but ≠ d.f: (غير الميم)

[1] Vasculature: ↑ No, ↑ Flow, VD.
  - ↑ NO & Flow of Blood in facial BV → Flushing.
  - Exaggerated VD response to: Hyperthermia.

[2] Climatic Factors: (sun)
  - Harsh climatic exposure (as Solar irradiation) → damage to Cut. BV & dermal C.T.
  - this explain why it:
    - Worsens in Spring & Summer.
    - affect Facial Convexities.

[3] Dermal Matrix degeneration & endoth. damage:
  - endothelial damage & dermal Matrix degeneration → Poor Tissue support of Cut. Vs →:
    - pooling of serum, inflammatory mediators & Metabolic wastes.

(dermal M. degen. ← leakage ← damage [مش عارفين انهي حصل الاول]
dermal Matrix degen. → lack of Vs support → endoth. damage. : ابدان

[4] Microbial organisms:

(a) Demodex: is a mite that NLLY inhabit the lumen of large Sebaceous follicles in areas affected by rosacea (Nose & cheeks); an immune response Mediated by T-helper surrounding Demodex is suggested (Controversy).

(it role is exacerbating Factor in predisposed individuals.)

(b) H. Pylori (Controversy).

(Ecfonethrin improves Erythema & Papules not Pustules.)

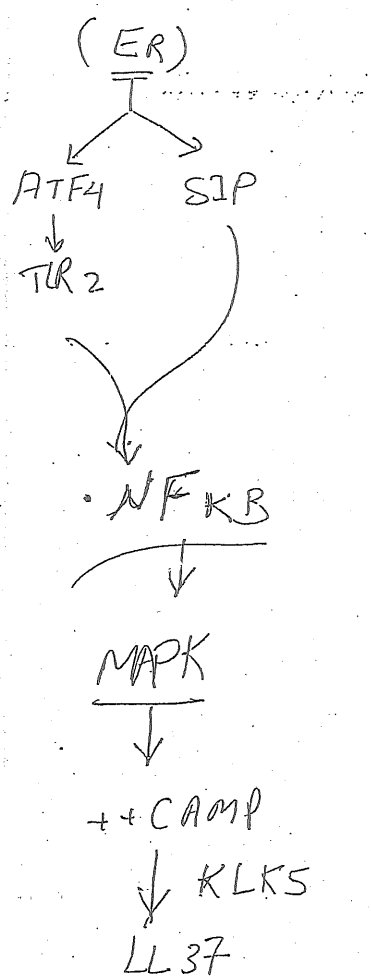
(c) P. acnes.

1. Vasculature
2. dessen.
3. Climatic
4. Chemical & ingested agents.

2. Microbes.
3. Antimicrobial peptides.

↑ ROS
↑ ferritin.

↓



- Metronidazole : -- Neut., ↓ ROS, -- KLK5
- Ivermectin : -- Demodex & MPAK
- Retinoids :

5. Anti Microbial Peptides: (AMPs): (2009) ↑↑

- def. Small MW proteins that are a part of innate. Immune response & have broad spectrum antimicrobial Activity against bact, viruses & Fungi. they are released upon injury & for inf.
- These AMPs are as:
  - Ⓐ Cantheli Cidins & β defensins → ↑↑ in Rosacea.
  - Ⓑ LL 37 (peptide form of Cantheli Cidin) is Expressed by PMNL & Lymphocytes → ↑↑ in Rosacea → interact ē Endothelial cell → ++ Angiogenesis.
    - Modulate VEGF Expression.
    - its injection in mice → inflamm, Erythema & Telangiectasia.

6. ROS: (2009)

- Neutrophils → ROS (superoxide anions, hydroxyl radicals, Singlet O., Molecular O, H_2O_2) → Tissue damage & inflammat°.

7. Serum ferritin:

- Fe → ++ Conversion of H_2O_2 to free radicals, ēv → Tissue damage & inflamm.
- Evidence of ferritin role:
  - Biopsy from rosacea → ↑ No of ferritin positive cells.

& higher ferritin positivity is ass. ē more advanced Types of Rosacea.

8. Chemical & ingested agents:

Spicy food, alcohol, hot beverages may Trigger Flushing (but these agents have No central role).

Peri vascular & perifolli cular inflamm. (Controversy).

- Epidemiology:
  - Age: → any (old & children) but Commonest 30-40 yrs
  - Sex: → ♀ > ♂
  - Race: More in Fair skin individuals.

C/P of Rosacea:

- **C/P Includes:**
  1- Features of Rosacea.
  2- Subtypes and variants of Rosacea.

1- PRIMARY AND SECONDARY FEATURES OF ROSACEA
A- Primary features
• Flushing (transient erythema)
• Non-transient erythema
• Papules and pustules
• Telangiectasia
B- Secondary features
2. Burning or stinging, especially malar skin.
3. Plaques
1. Dry appearance, especially central facial skin
5. Soft or solid facial edema
6. Ocular manifestations 40%
7. Peripheral location
4. Phymatous change

JAAD 2002

Burning
Stinging
Xerosis
Plaques
Edema.
Rhinoph.

(Important)

(1). Comparison bet Rosacea / AV

(2). Steroid Rosacea.

(3). LMDF

(4) Syndromic Acne.

- SAPHO
- PAPA
- PASH
- SAHA
- PCOS
- Follicular occlusion Triad or Tetrad.
- Apert.

2-SUBTYPES AND VARIANTS OF ROSACEA AND THEIR CHARACTERISTICS (National Rosacea Society 2002).

A- Disease subtypes :	Characteristics
1-Erythematotelangiectatic (Vascular)	Flushing and persistent central facial erythema with or without telangiectasia (Triggered by)
2-Papulopustular (inflammatory)	Persistent central facial erythema with transient papules and/or pustules (Lasting 1-4 ds)
3-Phymatous	Thickening skin, irregular surface nodularities and enlargement. May occur on the nose, chin, forehead, cheeks or ears (start as dilated pores Vs + wide pores → Progress)
4-Ocular	Foreign body sensation in the eye, burning or stinging, dryness, itching, ocular photosensitivity, blurred vision, telangiectasia of the sclera or other parts of the eye, or periorbital edema, recurrent styes & Chalazion.
B- Variants: 1-Granulomatous rosacea **2-Periorificial dermatitis** **3-Pyoderma faciale** **4-Steroid rosacea**	JAAD 2002

NB on CIP

(A) Erythemo Telangiectatic Type: (وردية وعروق)

Triggers
- Sun
- Emotional Stress
- Hot drinks
- Alcohol
- Spicy food
- Exercise
- Hot or cold weather
- Topical

- **Erythema:** . is the earliest sign.
  - . affect central face & Sparse periocular skin.
  - . acc. by stinging sensation
  - . start as intermittent → become long lasting than → persistent.
  - . skin is thin & lack Sebaceous quality (that Chic of Acne)
- **Telangiect.:** start at alae nasi → Nose → cheeks & may become large angiomas.
- **NB:** . Edema & induration is common.
  - . When Edema becomes persistent → woody induration occurs this is variant of Rosacea called: "Solid facial Edema, Rosacea Lymphedema (DD. that of AV).

(i). Erythema:
Early → Transient (Flushing)
Later → Fixed

(ii). Edema:
Early → Transient
Later → Fixed (Morbihan's)

(B) Papulopustular Type: (حبوب وبثور)

- the Classical Type.
- Papulopustules similar to that of AV but differs in:
  - . dome shapped.
  - . deeper red color.
  - . No Comedones.

(D) Phymatous Rosacea:

- d.t Seb. gland hyperplasia.
- Types:
  - clinically : Nasal & Extra nasal.
  - Histologically : (4)
    - glandular.
    - Fibrous.
    - Fibroangiomatous.
    - Actinic.

(E) Ocular Type:

ممكن تشخيص قبل الجلد بسنين ولكن اكثر الاحيان مرضان معاً.

- ..% of cut. rosacea show ocular S & S.
- Etiology: (1) Meibomian gland impaction → ↓ lipid content of tears → ↑ Evaporation → Eye irritability.
  (2) ↑↑ Matrix Metaloproteinase 9 in Tears (Doxy ↓↓ it → improvement).
  (3) Tear film Acidity (...)

Q Variants of Rosacea

1. Granulomatous Rosacea:

- Large granulomatous Nodules or Very persistent, discrete red to brown Facial papules That show granulomatous inflamm.
- May be overlaped c̄ LMDF. (lupus miliaris disseminatus Faciei) & Sarcoidosis
  الاسم الافضل

2. Perioral & periocular (Periorificial) Dermatitis: (Exel 2010)

"MIS-Diagnosed As perioral ECZema"

- def. chr. papulopustular & ECZematous Facial dermatitis usually affecting Women but ± also affect Children
- Etiology: unknown but ± d.t.:
  1. Topical Cs.
  2. Cosmetics: مرطبات الجلد - كريمات الاساس - معجون الاسنان
  3. Physical agents: UVRs, Heat, wind.
  4. Microbials: Fusiform bact, Candida, H. Pylori, Demodex ← Controversy
  5. Hormonal: Menestruation & OCPs
  6. GIT disturbance (Malabs).

"Y"

- Steriod:
  1. Acniform
  2. Rosacea
  3. Perioral Dermatitis

] "Overlap"

- monomorphous papules
- ± any pustules, scabs, ECZematous patches —

- <u>Epidemiology</u> : usually affects women 20–40 ys.
  - Children may be affected. (Childhood granulom. periorofacial D)
- <u>C/P</u> : • grouped "follicular reddish" papules, papulovesicles, pustules on Erythematous base that ± show confluence.
  - <u>Site</u>: • perioral (specially nasolabial) & periocular (lat. lower Eye lid) some times ē free border bet. the lesion & the vermilion boder of lips. "مميز"
  - Extra facial <u>involvement</u> may occur.

(Link to Rosacea is uncertain but: • Age & Histopath. ± similar • it ass ē Rosacea.)

- <u>NB</u>: Ttt ① <u>Stop the offending Agent</u>:
  ② <u>Tetracyclines, Topical Antib., Isot.</u>

وقف الكورتيزون فجأة قد يعمل هيجان ← يستعمل كورتيزون أقل كمية ثم وقف

• Tetra. استعمل

TIC ...

3 Pyoderma Faciale (Rosacea Fulminans):

(Linked to Rosacea d.t.: • Same path. • " Ttt.)

- sudden onset of:
  - Indurated plaques composed of grouped inflamed papulopustules at face.
- <u>it's similar to rosacea in</u>:
  - Pathology & Ttt
- <u>but differs from it in</u>:
  1. Younger Age.
  2. More often ♀
  3. No flushing.
  4. No ocular symps.
  5. Ttt (شكل) → Cs (40–60 mg/d). or <u>Isotretinoin, Antibiotic</u>

(M/S diagnosed as: • Pyoderma • leishmania • blastomycosis.)

4 Steriod Rosacea:

- occurance of Rosacea like lesions [or] Exacerbation of preexisting Rosacea in response to use of Topical Cs.
- <u>if Cs used in rosacea</u>:
  - <u>at first</u>: → improves.
  - <u>lateron</u>: → atrophy, persistent VD & inflammatory papules.

(NB) - <u>Rosacea</u> like lesions at upper lips + ala nasi → clue of Cs use.

(H) ① Stop Cs : [فجأة أو تدريجيا]
② Topical Parmoxine " non sensitizing local anaesthetic "
③ Soothing agents.
④ Topical Calcineurin inhibitors — على الرغم سارتنا عكس "Rosacea & ↑ Demodex Prolif."

. Add weaker Cs then Stop.
. Add Doxy.
← Flare لو حصل وقف الكورتيزون فجأة.

• Histopathology of Rosacea:

① Mild: → Vascular Ectasia & mild Edema of papillary dermis
② Advanced (Non pustular): perivascular & perifollicular lymphohistiocytic infilt.
③ pustular: Granulomatous inflamm. & ± perifollicular abscess (non Caseating Epitheloid).
④ also ✓. ↑ Demodex.
✓. Seb. Hyperplasia.

• DD. of Rosacea:

① AV.
② SD.
③ L.E
④ LMDF
⑤ Haber Synd.
⑥ Demodex Folliculitis.

1. AV: younger age, ♂ = ♀, Comedones & Cyst, not exactly in central face & Trunk, greasy skin
2. SD: greasy Scales at Seborrheic Sites. Sq. blepharitis may Simulate ocular Rosacea.
3. LE: Malar Erythema but no papulopustules.
4. LMDF: "lupus Miliaris disseminated Faciei" (See below)
5. Haber Synd. (See below).
6. Erythemotelangiect. Rosacea → Dermatoheliosis.
7. Periorificial Dermatitis → Perioral ECZ. / Periorbital ECZ.

- Haber Synd:
  - AD condition, some times overlap ē Dowling-Degos.
  - C/P:
    - Early life: Persistent Rosacea like facial Eruption.
      ± Comedones & pitted atrophy.
    - Later on: Keratotic Follicular Papules on Trunk & Extremities.

"FIGURE"

Lupus Miliaris Disseminatus Faciei (LMDF)
(Acne agminata) = Acnitis.

Def.: an uncommon, chronic, inflammatory dermatosis characterized by red-to-yellow or yellow-brown papules of the central face, particularly on and around the eyelids.

Etiology and pathophysiology: Uknown but may be due to : React=

1-Tuberculid reaction to MYCOBACT.-TB.

2-reaction to Demodex folliculorum.

3- granulomatous reaction to hair follicle destruction or ruptured epidermal cysts.

Epidemiology: more in asian Young males(20^{th}). (♂>♀)

C/P: Lupus miliaris disseminatus faciei (LMDF) manifests red, brown, or yellow-brown papules that appear singly or in crops. The papules appear on the central face, especially on and around the eyelids of young adults. They are found predominantly on the face in areas traditionally affected by rosacea.

Lesions occasionally may be generalized and appear on the extremities or trunk. Axillary lesions may be mistaken for antiperspirant-related granulomas. Lesions may present later as crusts, pustules, and, ultimately, scars. ⟷ Pitted (Pox like) Scars.

Pathology:

Early: lupus miliaris disseminatus faciei (LMDF) lesions show superficial perivascular and periappendageal lymphocytic infiltrates with a few histiocytes and neutrophils.

Fully developed lesions: show round granulomas, often with caseation necrosis.6 The changes mimic miliary tuberculosis. Mixtures of sarcoidal and tuberculoid granulomas also may be seen. Late lesions show fibrosis with scattered lymphocytes, histiocytes, and neutrophils and also may be perifollicular and may show epidermal thinning.

(i). Early:
(ii). Fully developed
(iii). Late: Fibrosis

TTT:

(1) Medical: A variety of medical treatments reportedly are effective in lupus miliaris disseminatus faciei (LMDF), although controlled studies that support one treatment or group treatments as optimal are lacking. Reported therapies include the following:
Low-dose prednisone,Intramuscular triamcinolone,Dapsone, Tetracycline products
Antimalarials ,Pyridoxine hydrochloride,Riboflavin,Isotretinoin

(2) Surgical: * Scar revision procedures.
* 1450-nm diode laser and Pulse-dye laser.

NB: - Demodex Folliculitis: Rosacea like facial Erupt= may occurs in Immuno Compromised patients (HIV & leukemia). # → ??